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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

CONGENITAL DEFECT OF ABDUCTION ASSOCIATED WITH RETRACTION OF THE EYEBALL.

By John T. Carpenter, M.D.,

Lecturer on Ophthalmology at the University of Pennsylvania; Attending Ophthalmic Surgeon to the Bryn Mawr Hospital.

Under the above title may be grouped a rare and interesting muscular anomaly, presenting clinical signs so constant and characteristic as to deserve consideration as a distinct ocular syndrome.

Since Heuck's[1] description in 1879 about 31 cases have been reported. In the *Ophthalmic Review* for 1903 Evans summarizes in a table the important points gleaned from the literature of 27 cases, including 2 added by himself, from which the following data have been taken:

While the condition is undoubtedly congenital, yet, owing to the absence of symptoms, patients are often not brought to the surgeon for some years after birth. Females are usually affected (11 females, 5 males, 8 no sex mentioned), and the left eye is almost invariably the one at fault (20 left, 4 right, 3 bilateral).

The visual acuity was normal or became so with glasses in 9 cases; was reduced one-half to one-tenth in 6 cases; there was amblyopia in 2 cases; while the visual acuity was not mentioned in 10 cases.

In the primary position the ocular axes may be parallel, divergent, or convergent, or there may be vertical deviation. In 27 cases the relation of the ocular axes in the primary position was noted as follows:

Parallel	10
Divergent	7
Convergent	5
Not mentioned	4
Downward	1
	27

There may also be well-marked narrowing of the palpebral fissure, and the affected eye may look smaller and sunken—enophthalmos.

Abduction is almost invariably absent, and with this is often associated defective convergence—which may, indeed, be replaced by conjugate movement toward the affected side—and we may find no "convergence reaction" of the pupil. But the most remarkable features of this affection are revealed by attempted conjugate movement. When the patient attempts to turn the eyes toward the *unaffected* side, the affected eye in place of inward movement is drawn back into the orbit, accompanied by a narrowing of the fissure. There may be associated upward or downward rotation, which has been regarded as the result of the counter-pressure of the optic nerve acting on a higher or lower plane than the retracting muscles (Wolff[2]).

On attempted movement toward the *affected* side, the palpebral fissure widens, the eyeball comes forward until it is as prominent as its fellow-eye, but no rotation beyond the median line results—this representing the complete relaxation of the internus. Homonymous diplopia is now noticed in many cases, but binocular single vision may be found with the eyes in the primary position.

Passive traction with conjunctival forceps usually shows entire absence of outward movement, with occasional limitation of inward rotation.

Subjective symptoms may be entirely wanting, or the patient may complain of headaches, diplopia, and the usual disturbances due to double vision.

"That these headaches are due to oft-repeated retraction of the globe and the consequent pressure on the orbital contents I feel certain," says Wolff.[2] "If anyone will repeatedly push back his eye into the orbit for half or three-quarters of a centimetre, he will experience an unpleasant sensation of pain."

In the case of the patient reported by the author this symptom was most prominent.

The notes of the case which I wish to report are as follows:

Mrs. H., aged forty years, of Warren, Ohio, consulted me March 1, 1902, on account of severe long-standing headaches, diplopia, and disturbed general health, owing to reflex nervous disorders, which she attributed to the condition of her eyes. She had always been so morbidly sensitive because of the "sunken appearance" of her left eye that she had never before consulted an ophthalmic surgeon. From her earliest remembrance she had carried her head tipped toward the right shoulder, with her face turned well toward the left to lessen her annoying double vision.

Visual acuity: O. D., 6/6; O. S., 6/6. Refractive error, measured under complete cycloplegia: O. D., + 0.25 cx. 90°; O. S., + 0.25 cx. 90°. Inspection revealed the characteristic appearance of enophthalmos, best likened to the wearing of an artificial eye.

In the primary position there was convergent strabismus of about 6 degrees and extremely slight narrowing of the palpebral fissure. Maddox rod showed 12 degrees

[1] Klinische Monatsbl. f. Augenheilk., 1879, p. 250.

[1] Archives of Oph., 1900, p. 297.

[2] Loc. cit.

esophoria, 2 degrees right hyperphoria. Candle field revealed diplopia to the left of the median line; the distance between the false and the true image increased as the candle was carried to the left, and the images were on the same level, except in the extreme lower left portion of the field, where the false image fell below the true and seemed nearer the patient.

In fixing with the affected eye there was marked secondary deviation of the right eye down and in.

The movements of the right eye were normal in all directions.

The affected eye could move outward 2 mm. beyond the middle line; inward movement somewhat restricted; the cornea could not be carried to the inner canthus; upward movement was normal, with slight restriction downward.

FIG. 1.—Shows narrowing of the palpebral fissure, sinking of the eyeball (enophthalmos), and defective inward rotation of the left eye when patient looks toward the unaffected side.

Conjugate movement toward the *unaffected* side resulted in increased enophthalmos, with restricted movement of the affected eye; while movement in the opposite direction produced decided lessening of the enophthalmos, but the affected eye failed to move outward beyond the midline. Convergence near-point was 8 cm. from the root of the nose.

In all these movements there was very slight alteration in the width of the palpebral fissure.

After correction of her presbyopia Mrs. H. became much more comfortable and refused any attempt at surgical interference, and in June, 1904, reported that her general health had greatly improved since using the glasses. Examination at this time brought out no new facts, except that the left eye was found rigidly fixed as regards passive inward movement, being apparently held by an inextensible external rectus.

Pathological Anatomy. Lawford has said that the defect in all these cases lies in the muscular and not in the nervous structures, and in some of the reported cases operative interference revealed the following conditions:

1. The external rectus muscle was found to be reduced to a fibrous and more or less inelastic band.
2. No external rectus muscle was found.
3. The external rectus tendon was inserted far behind its normal position.
4. The internal rectus was found similarly displaced.
5. A marked shortening of the recti muscles was demonstrated in some cases.
6. Retracting bands were found associated with the internal rectus in two cases.

Especially interesting is the case reported by Knapp,[1] in which the internal rectus was found very thick, its insertion

FIG. 2. Shows failure of left eye to turn out in looking toward left, but enophthalmos replaced by propulsion and widening of palpebral fissure.—(*From Evans' article, Ophthalmic Review*, 1903.)

reaching downward almost to the inferior rectus. Following the tenotomy no lessening of the enophthalmos occurred until the further division of bands, which were inserted posteriorly. Immediately upon division of these bands the eyeball protruded and moved neither inward nor outward. As Knapp remarks: "The operation seemed to demonstrate something like a retractor muscle as found in some animals."

Tuerk, of Berlin,[2] first explained the symptoms presented in this interesting clinical picture on the basis of the "faulty insertion" and the "fixation" theories.

"According to the faulty insertion theory, the retracting muscle, which is the internal rectus, is attached to the eyeball farther back than normal. Consequently the por-

[1] Archives of Oph., 1900, p. 311.

[2] Centralblatt f. prakt. Augenheilk., January, 1899, and Deutsche med. Wochenschrift, 1896, No. 13.

tion of muscle capable of unwinding itself from the globe is diminished, and inward rotation is correspondingly replaced by a backward pull on the globe when the internal rectus contracts." This theory is supported by anatomical conditions revealed by operations and dissection, but does not satisfactorily account for the entire loss of function of the external rectus invariably found in these patients.

The fixation theory assumes "that the paralyzed external rectus consists of an unyielding connective-tissue strand in place of elastic muscle fibres. It, therefore, fixes the eyeball on its outer side and offers an obstacle to adduction, so that the eye can yield to the traction of the internal rectus only by moving back into the orbit at the same time that it turns inward."

The following extract from a personal communication to the writer by Alexander Duane is a clear and comprehensive statement of the various hypotheses advanced to explain this peculiar syndrome:

"1. That the externus is replaced by an elastic or inelastic strand of connective tissue. If elastic it would give when the internus contracted, if inelastic it would not. In the latter case not only would the movements inward be hampered, and hence deficient, but, in fact, it could not take place at all *unless the eyeball also retracted.*

"2. That the internus is inserted too far back, acting thus as a *retractor.*

"3. That the internus is normally inserted, but has an additional slip far back, acting as a retractor.

"4. That besides '2' or '3' there is deficiency in the check ligaments, which would, when the internus contracted, allow the eye to sink back into the orbit.

"5. That the superior and inferior recti, acting very strongly (as adductors) to replace an inefficient internus, also pull the eye back."

"Hypothesis '1,' I believe, is the one that holds good in the majority of cases, although in some '2' or '3' have been shown to be present by actual dissection, and in some other cases they were probably present.

"Hypotheses '4' and '5' have no anatomical proof and there are several reasons for thinking that '5' cannot be the cause.

"The oblique upward or downward movement of the eye observed in many of these cases, when the attempt at adduction is made, is, I believe, due to spasmodic action of one of the obliques. It cannot be due to extreme action of either the superior or inferior rectus, for these muscles, when the eye is adducted, act very slightly as elevators. Nor do I think it can be adequately explained by supposing a peculiar insertion of the internus, so that the latter acts as an elevator or depressor; nor by assuming, as Wolff does, that it is due to the counter-pressure of the optic nerve crowded against the eye as it is retracted.

"The closure of the palpebral fissure, which often occurs to a marked degree when the eye is adducted, cannot be ascribed, as has been done, to the enophthalmos, giving rise to a loss of support for the lids, for it occurs in cases in which there is no enophthalmos. It is probably produced by some peculiar synergy between the third nerve and the facial."

Treatment. Treatment, if attempted at all, should be undertaken for cosmetic purposes. The enophthalmos has been to quite a large extent removed by free tenotomy of the retracting muscle. Advancement of the internal rectus, to cure the divergent strabismus sometimes present, invariably results in an increase in the retraction of the eyeball. "The proper proceeding," says Wolff,[1] "provided an operation is indicated, would be a tenotomy of the retracting muscle with fixation of the globe in the opposite position to ensure an effect. In this way the squint and the retraction of the ball would be improved, although some motility would be sacrificed."

Bibliography.

See Evans' article, Oph. Review, 1903.
Additional cases reported:
Schapringer. Die Oph. Klinik, December 5, 1901, p. 359.
Spuler. Klin. Monatsbl. f. Augenh., September, 1903.
Koeber. Three Cases of Retraction Movements of the Eyeball, La clin. ophtalmol., October, 1903.

[1] Loc. cit.

ANEURYSM OF THE DESCENDING THORACIC AORTA, CAUSING EROSION OF THE VERTEBRÆ AND SYMPTOMS SIMULATING POTT'S DISEASE.

By Charles W. Burr, M.D.,
Professor of Mental Diseases, University of Pennsylvania.

The percentage of cases of aortic aneurysm in which vertebral erosion occurs is small. It is least frequent when the aneurysm is situated in the ascending portion of the arch and most frequent when it is in the descending thoracic or abdominal aorta. In the cases in which erosion has taken place death usually occurs before the bony absorption has progressed far enough to cause symptoms referable to the spinal cord or visible and palpable deformity of the spine. When the aneurysm is so situated as to develop without producing characteristic physical signs and symptoms and

has progressed so far as to lay bare the spinal membranes and to set up a compression myelitis, Pott's disease, a tumor of the vertebræ, or a solid tumor not arising in but encroaching upon the spine, may be believed to be present. For anatomical reasons the diagnosis is most difficult, and mistakes are most likely to be made if the aneurysm has its origin in the descending thoracic aorta.

In the following case I was led into error by the slight pain, the marked kyphosis, the presence of the tuberculin test, and by the fact that the symptoms of which the patient complained were entirely spinal. There were, of course, no physical signs of aneurysm. It was thought of, considered, and excluded. Had I, however, continued to examine the patient's back at intervals a correct diagnosis could finally have been made, because at the necropsy there was present a posterior bulging of the ribs of a kind never met with in Pott's disease. This must have developed only a short time before death, because I only ceased to examine him when I was sure that to have him propped up in bed would seriously injure him. I ought to have given more thought to the duration of the disease before he came to the hospital, because it is very unusual for Pott's disease to run such a long course before spinal-cord symptoms become manifest.

The man's history is as follows: He was a laborer, aged fifty-six years, who was admitted to the Philadelphia General Hospital October 15, 1902. He stated that many years before he had had syphilis and also malarial fever, but never any other illness. His present trouble began with dull rheumatic pains in the back four years before his admission to the hospital. Sometime later the left leg and then the right became numb. Still later both legs slowly became stiff, but he only ceased to be able to walk two days before coming to the hospital. Two weeks before he began to have urinary incontinence.

Examination. He lay in bed with the legs rigidly flexed on the thighs and the thighs on the abdomen. Both knee-jerks were very much increased and ankle clonus was present on both sides. Stroking the right sole caused flexion of all the smaller toes, the great toe remaining motionless. Stroking the left sole sometimes caused flexion, sometimes slow extension of all the toes. A prick anywhere on either leg caused it to flex. The Achilles jerk was marked on both sides. There was slight atrophy of the right calf and still slighter of the left. There was only partial control of the bladder and rectum. There was slight angular curvature over the eighth dorsal vertebra. There was no posterior bulging of the ribs. Pressure on the spine at the seat of deformity caused pain. He complained of pain in the back which he could not localize further than to say that it was worse under the right scapula. The arms were normal. The right leg was anæsthetic. The left was sensitive to deep pressure, but not to touch. There was not a clear-cut line on the abdomen separating the anæsthetic area from that in which sensibility was retained, but at the level of the umbilicus there was a band about two inches wide in which sometimes he felt and sometimes he did not feel touch. Below the crests of the iliæ there was complete tactile anæsthesia Speech was normal and he had no difficulty in swallowing. The pupils were equal, moderately dilated, and reacted well to light and with accommodation. Respiration was normal and there was no cough. The radial pulses were synchronous. His temperature ranged from 98° to 100°. The urine was alkaline and contained a little pus, a trace of albumin, but no casts. In other words, there was chronic cystitis. Examination of the chest was negative. He was given a tuberculin injection and a distinct reaction followed. Some days before death, on March 23, 1903, bed-sores appeared upon the buttocks and the temperature ranged between 100° and 103°. The necropsy was made by Dr. Joseph McFarland. There was quite marked bulging of the thorax posteriorly on the left side and moderate kyphosis. A large aneurysm was found beginning at the descending portion of the arch and extending to the level of the tenth thoracic vertebra. The aneurysmal sac contained two large organized masses each about the size of the fist. The bodies of the thoracic vertebra and the intervertebral disks from the fourth to the tenth inclusive were completely eroded, exposing the spinal canal. The spinal dura was adherent to the posterior wall of the aneurysm throughout this distance. The left pleural cavity was filled with blood which had come from a rupture of the aneurysm. The heart was normal. There was no sign of tuberculosis in any of the viscera. Of course, there may have been tuberculous foci so small as to have been overlooked.

Dr. D. J. McCarthy made a microscopic examination of the spinal cord and reports as follows: "On gross examination the dura showed very marked external meningitis extending from the fifth to the tenth dorsal segment, most extensive on the anterior aspect of the cord, but in some areas involving almost three-fourths of its circumference. Within the dural cavity was some extravasated blood and on the inner surface of the dura was a whitish membrane about 2 mm. in thickness."

"Sections from different segments of the cord were studied after being stained by the Weigert sheath stain, the Nissl, the iron hæmatoxylin, the Marchi method, and the combined nuclear and connective-tissue stains.

"The Marchi method showed in the segment above the eighth dorsal an irregularly typical ascending degeneration. The degeneration was marked in the entire posterior columns below and narrowed to the posteromedian columns above. Degeneration was marked in the direct cerebellar tract on the left side and slight on the right. Below the eighth dorsal segment there was marked degeneration of the crossed pyramidal tracts. In the anterior columns there were found black granules scattered here and there, but not only in the direct pyramidal tract. A distinct band of these granules extended from the anterior median fissure along the periphery

of the cord to the exits on the anterior roots as far down as the lower lumbar segment. The results obtained by the Weigert method corresponded in general to those of the Marchi method. Where the dura was most diseased sections showed masses of free red blood corpuscles within the dura and in the interstices of the true and false dural membranes. The Nissl method showed in the lower dorsal region some slight chromatolytic changes, but elsewhere throughout the cord, and especially in the lumbar cervical enlargements, nothing abnormal was seen. Study of the dural membranes and cord by the haemalaun method showed the following conditions: The cord, even at the point of greatest pressure, showed no signs of inflammation. There was, however, at the level of the eighth dorsal segment, a spot of softening. Within this area was a diffuse degeneration of the cord, with dropping out of the axis cylinders, giving a reticular formation. The gray matter was with difficulty differentiated from the white, and the anterior gray cells had almost entirely disappeared. Those which remained were in an advanced stage of chromatolysis. By the Marchi method extensive degeneration was shown throughout the entire area. There was a slight degree of round-cell infiltration. The dura itself was somewhat thickened, with here and there accumulations of small nuclei in the interspaces. The new membrane on the external surface of the dura was very rich in small round cells surrounded by a stroma of delicate connective-tissue fibrils. It also contained many newly formed bloodvessels and many free red blood cells. The internal false membrane was also very rich in cells, but of a somewhat different type. The connective-tissue fibrils, while most delicate, were also more numerous than in the outer membrane and formed a close reticulum. The cells most frequently seen between the fibrils were of a much larger size, with small nucleus —*i. e.*, were epithelioid. They were most numerous about the vessels, indeed, were the only cells there. Many capillaries were present. The larger cells were evidently derived from the lining cells of the pia-arachnoid. To sum up: there was an intense proliferating chronic internal and external pachymeningitis of the dorsal cord. Within the cord above and below the point of greatest pressure ascending and descending degeneration was present. The degeneration in the margin of the anterior columns was not that found in the ordinary type of secondary degeneration."

The age of the patient is of no diagnostic value in an obscure case of compression myelitis, because Pott's disease, though most frequent in childhood, may occur even in old people. I have met with it in a man seventy years old. He had been sometime in the almshouse, complaining only of a little stiffness in walking and frequency of micturition. One day he found he could scarcely get out of bed on account of weakness in the legs and was transferred to the hospital department. He very rapidly lost power entirely in one leg and partly in the other. One leg was anæsthetic up to the groin, in the other the anæsthesia ceased at about the knee. There was incontinence of urine. The knee-jerks were but little exaggerated. There was neither spinal deformity nor spinal pain. He had moderate fever. He died a few days after admission. At the necropsy the body of the third dorsal vertebra was found to be carious. There was some external meningitis and consequent pressure myelitis, chronic cystitis, and pyelonephritis, and resulting therefrom septic pneumonia, which had caused death. The vertebral disease was tuberculous and not a septic abscess.

Mistakes are most likely to occur in cases in which the aneurysm causes no symptoms until the erosion of bone has progressed so far that pressure myelitis results, and the only symptoms present are referable to the spinal cord. Local or referred pain is, as a rule, an early symptom in aneurysm, but it may be absent entirely. Local spinal pain and tenderness is an early symptom of Pott's disease, whereas the early pain of aneurysm is apt to be referred to some other region than the spine. The region to which the pain is referred will depend upon the nerve cords pressed upon. It may be paroxysmal or continuous, sharp or dull, local or diffused. Depending on the location of the aneurysm it may be felt in the chest, the abdomen, the left arm, the legs, the penis, or rectum. There may be anæsthesia in the distribution of the nerves in which pain is felt. The seat of pain may vary from time to time and the anæsthesia may disappear and reappear with variations in the amount of pressure on the nerves. This variability may lead to the error of supposing that the pain is hysterical. Again neuritis may be thought to be local and primary when it is really due to aneurysmal pressure. For example, a neuralgia of the left arm from aneurysmal pressure has been supposed to be caused by primary disease of the nerve trunks. Indeed, the pain of aneurysm may lead one far astray if its cause be not carefully looked for and found. It may simulate that of renal calculus, gallstone, and even the girdle pain of locomotor ataxia. Sudden violent pain in the trunk accompanied with spasm and palsy in one or both legs is almost always caused by the rupture of an aneurysmal sac into the spinal canal. Sudden paraplegia may occur late in Pott's disease, from the giving way of the carious vertebræ and a consequent sudden increase of pressure from displaced bone; but, as a rule, the spinal-cord symptoms come on more or less slowly and result from the pressure of the meningeal exudate. Most rare of all in Pott's disease is the sudden appearance of palsy in a person who previously presented no symptoms. Many years ago I saw the late Dr. Carl Weigert make a necropsy on a young man who suddenly fell dead and in whom was found tuberculosis of a cervical vertebra in which spontaneous fracture had occurred. His relatives had never heard him complain of being ill or even unwell.

Theoretically symptoms of nerve compression should precede any evidence of involvement of the spinal cord in aneurysm. But sometimes signs of compression of the cord

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are the first and only symptoms. The cord symptom may be sudden or slow in onset and may or may not be associated with spinal deformity. The latter may be identical with the kyphosis of Pott's disease or, with the curvature, the ribs may bulge markedly on the left side. A bruit may be audible over this region. As just said, the cord symptoms may be sudden or slow in onset. There may be a sudden clonic spasm of one or both legs, followed by palsy or a sudden or slowly oncoming palsy of the legs. Thus in one case, after a gradual loss of power in both legs, there was sudden severe pain in both groins and both legs, with such severe spasm in the left that the heel was drawn up to the nates and there fixed. An hour later the spasm relaxed and the leg was paralyzed. Similar spasm recurred till death several months later. Rarely both legs and arms may be palsied. Palsy may be present without anæsthesia, but the reverse cannot occur.

It is rather remarkable that Pott's disease, notwithstanding the great deformity of the spine and the inflammatory processes set up, so rarely causes disease of the aorta. A few cases are recorded in which a false diffused aneurysm of the aorta has resulted from caries. The earliest case I have found after a cursory search is one by Edward Dewes, in the *London Journal of Medicine*, 1852, vol. iv. p. 35. In it the abdominal cavity on either side of the spinal column was occupied by a large mass consisting of extravasated blood, lying in the cellular membrane behind the peritoneum, and following the psoas muscle as far as Poupart's ligament. The aorta in front of the ninth and tenth dorsal vertebræ was slightly enlarged, its coats thickened, but not containing any coagulated lamina, nor was there any distinct sac. The mass was strongly adherent to the vertebræ. The bodies of the ninth and tenth dorsal vertebræ were nearly destroyed by caries and the bodies of the eighth and eleventh were somewhat affected. The interarticular cartilages were intact. Exfoliation had occurred and several pieces of bone were found among the coagula. On laying open the aorta a circular opening the size of a shilling, the edges firmly attached to the bone, and interarticular cartilages, was found.

Aneurysm can only cause pressure upon and compression myelitis of the cord, and hence cannot produce a clinical picture of any of the systemic diseases of the cord. It is true that in locomotor ataxia aneurysm is more frequent than in the general population, but the two diseases run their courses independently of each other, and, of course, neither is causative of the other. When in the course of locomotor ataxia an unsuspected aneurysm erodes the vertebræ and sets up a myelitis, the clinical picture may be so complicated that a correct diagnosis cannot be made unless the man's previous nervous symptoms are known. It is possible that in some of the cases of alleged trophic disease of the vertebræ occurring in locomotor ataxia, in which the diagnosis was based on spinal deformity and not verified by autopsy, the change was not trophic but aneurysmal erosion. Syphilis plays such a large part in the causation of both locomotor ataxia and aneurysm that their frequent association is not surprising. So far as my personal experience goes, aneurysm is infrequent in spinal syphilis—I mean in true syphilitic meningomyelitis, in which pathologically the process is really specific, and not merely parasyphilitic.

ON THE INFLUENCE OF COPIOUS WATER DRINKING.

By P. B. Hawk, Ph.D.

(From the Laboratory of Physiological Chemistry of the Department of Medicine of the University of Pennsylvania.)

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I. HISTORICAL SUMMARY.

A large number of investigations have been made for the purpose of obtaining data relative to the effect produced upon the metabolic processes by the drinking of large volumes of water. The influence of the entire or partial withdrawal of water from the diet has been made the subject of a smaller number of investigations. The number of observations upon increased and decreased water ingestion being so great and the diversity of experimental evidence upon the subject being so pronounced, we have deemed it expedient to make a rough classification of the various investigators according to the experimental methods adopted and the nature of the conclusions reached. Not all the experiments we shall mention were made for the purpose of studying the influence of any particular modification in the water ingestion. However, in several instances, notwithstanding the fact that the primary object of the investigation was entirely foreign to the subject we are considering, yet the conditions under which the observations were made were fortunately such as to allow us to draw definite conclusions regarding the influence of an increase or a decrease in the volume of water taken into the body. The data obtained by the same investigator at different times and under varied conditions may indicate opposed conclusions regarding the influence of altered water ingestion, and in such instances a single observer may be included in more than a single division of our classification.

We will place in our first class numerous investigators from whose data we are enabled to draw the conclusion that water in small or large amount, when added to the diet, causes at least a slight increase in the excretion of nitrogen by the urine. Of the members of this class, Voit,[1] Panum,[2] E. Salkowski,[3] Feder,[4] Falck,[5] and Munk[6] used normally fed animals, generally dogs. Voit observes that the addition of water in increased amount to the normal diet facilitates metabolic activity, and at the same time stimulates proteid catabolism and increases the volume of the urine. The same author reports an increased excretion of nitrogen after the ingestion of a large amount of water by a fasting animal. Panum fed a dog for forty-eight hours on a uniform diet of meat and bread, the animal being allowed no water. Under these conditions the curve for the excretion of urea following the ingestion of food rose slowly, and one-half of the urea excretion for a period of twenty-four hours after a meal was excreted during the first eleven hours. If the dog was given no water for a period of seventy-two hours the increase in the excretion of urea, following the taking of food, ceased after an interval varying from one to four hours in length; whereas when the animal had been allowed no water for seventy-two hours and was given 500 c.c. of the fluid twelve hours after the last meal, and at a time when the course of the urea excretion was approximately uniform, a small increase in the urea excretion was noticed, and this increase was accompanied by a much more pronounced rise in the volume of the urine. The observations of Panum indicate that when water is withheld from a diet otherwise normal, the customary marked variations in the rate of the nitrogen excretion following the ingestion of a proteid food do not occur.

E. Salkowski, by means of a series of experiments upon normally fed dogs, secured data indicating that an increase in the amount of water ingested produces a very small or entirely negligible increase in the excretion of nitrogen by the urine. Feder cites an instance in which, upon a uniform diet and with the volume of water ingested increased from 300 c.c. to 600 c.c. after the excretion of urea had become fairly constant, an increase of about 4 grams in the urea excretion was noted on the first day after the large volume of water was taken, and on the second day, while still maintaining the increased water ingestion, a decrease in the urea to slightly below normal occurred. In a later paper he concludes that the increase in the excretion of nitrogen after the ingestion of water in anything but an enormous amount is entirely insignificant. Falck, by increasing the water in the diet of a normal dog 500 c.c., observed an increase of from 0.5 to 1 gram in the urea excretion.

From data given by Stohmann, Rost and Frühling,[7] from experiments upon goats; Weiske, Kennepohl and Schulze,[8] from experiments upon sheep; Bartels,[9] Smith,[10] Meyer,[11] Winternitz,[12] Edsall,[12a] Mosler,[13] Weiske,[14] Kaupp,[15] Rosemann,[16] Böcher,[17] Bidder and Schmidt,[18] and Ter-Grigorianz,[19] from experiments of various orders, virtually the same conclusions may be drawn as those advanced by the investigators named above. In one experiment Weiske, Kennepohl and Schulze secured an increase of 0.6 gram of nitrogen upon increasing the water in the diet of a sheep from 630 c.c. to 1910 c.c. In a second experiment these same investigators obtained an increase of 1 gram in the nitrogen excretion upon raising the amount of water ingested from 960 c.c. to 1650 c.c.

As the result of experiments upon dogs, Meyer concludes that following an increased consumption of water, the urea and other more highly organized nitrogen-containing bodies are washed out from the tissues and that as a result of this the nitrogen content of the urine is raised. He believes, however, that an increased excretion of nitrogen does not necessarily accompany an increase in the volume of the urine. Weiske, in a series of experiments upon sheep, in which he studied the influence of the ingestion of sodium chloride and water, found the excretion of nitrogen to vary directly with the amount of sodium chloride and water ingested. Ter-Grigorianz, from a series of four experiments upon healthy human subjects, concludes that increased consumption of water stimulates proteid catabolism.

There are a number of investigators whose data seem to indicate a much more pronounced increase in the excretion of nitrogen by the urine, following the addition of large vol-

umes of water to the normal diet, than the data from the experiments of the observers already mentioned appear to indicate. Among the promoters of this order of investigation we may mention Rubner,[20] Forster,[21] Becher,[22] Schöndorff,[23] Salkowski,[24] Eichorst,[25] Weigelin,[26] and Genth,[27] all of whom we will include in our second class. Rubner's experiments upon fasting rabbits were planned so that the animals received no water for several days, and this total withdrawal of the fluid was followed by a period when the animals were allowed water *ad libitum*. During this second period Rubner found that the excretion of urea was nearly twice as large as it was during the period when the animals were entirely deprived of water. Following an addition of 1828 c.c. to the amount of water consumed by a dog, Forster observed an increase of approximately 10 grams in the excretion of urea. According to Becher, a period of three days was necessary to again assume the normal rate of nitrogen excretion after a considerable increase following a large addition to the volume of water ingested. Schöndorff, as the secondary part of an investigation which had for its primary object the study of the influence of an increase in the consumption of water upon the excretion of uric acid, observed the course of the nitrogen excretion under the conditions mentioned. He increased the volume of water ingested by amounts varying from 2 litres to 4 litres per day and secured an increase approximating 2 grams in the excretion of nitrogen upon the days when the ingestion of water was augmented.

The object of Eichorst's experiments was entirely foreign to the field of our investigation, yet we find some interesting points in his discussion. Finding the amount of urine eliminated by the dog upon which he was experimenting to be quite insufficient to allow accurate determinations of the various kinds desired, the author decided to increase the amount of urine by giving the animal large quantities of water at intervals. The dog was allowed no food for three days. On each of the five days following the animal received 68 grams of white bread, and water in varying volumes up to 800 c.c. The amount of urea excreted seemed to vary quite regularly with the volume of water consumed. The rise in the amount of urea excreted from 1.8 grams on the next to the last day when no water was taken, to 8.5 grams on the last day, simply by the addition of 800 c.c. of water to the diet, is very striking. Weigelin, in the course of an investigation upon the excretion of urea during and after muscular work, found that when the amount of water taken was increased the urea output was raised from 5 per cent. to 45 per cent. above the normal rate.

Genth, as early as 1856, from experiments upon himself, drew the conclusions that drinking large volumes of water caused a marked increase in the excretion of urea, a proportionate increase in the excretion of sulphate, and a small increase in the excretion of phosphates.

We are inclined to include Bischoff[28] and Foster[29] in the list of investigators who believe that water added to the normal diet in large volume may cause a correspondingly large increase in the excretion of nitrogen by the urine. The former observer states that water exercises before all other agencies, apart from the nitrogen content of the food taken, the greatest influence upon the excretion of urea by the urine. Foster, in his *Text-book of Physiology*, says: "Water has an effect on metabolism, as shown, among other things, by the fact that when the water of a diet is increased the urea is increased to an extent beyond that which can be explained by the increase of fluid increasing the facilities of mere excretion."

In addition to those enumerated in our classification there are several investigators whose work cannot properly be included in either of the classes mentioned. Henneberg,[30] for instance, concludes, from his experiments made upon oxen, that an apparently permanent increase in the nitrogen excretion occurs upon the continued consumption of large volumes of water. Opposed to Henneberg we find Oppenheim[31] and Neumann,[32] who put emphasis upon the claim that no such permanency in the excretion of nitrogen occurs as a result of prolonged, increased water ingestion. Oppenheim conducted his experiments upon increased water consumption in connection with experiments having for their aim the determination of the influence of muscular work, quinine, coffee, etc., upon the excretion of urea. The diet used was entirely normal and uniform throughout the course of the experiments. After securing a condition of approximate nitrogen equilibrium, 4 litres of water were added to the constant diet, 2 litres being taken at 1 o'clock in the afternoon, 1 litre at 5 o'clock, and the remaining litre at 9 o'clock in the evening. Following the ingestion of the 2 litres after the mid-day meal there occurred the surprisingly large increase of 6 grams above normal in the excretion of urea, whereas during the next four hours, notwithstanding the consumption of an additional litre of water, the excretion of urea fell below normal. A slight increase above the normal was noted with the addition of the fourth litre of water, but this increase was followed by a period during which the excretion of urea remained slightly below normal. In falling below normal after the initial rise induced by an increased water ingestion, the courses of the urea excretion in the experiments of Feder and Oppenheim are notably similar. The author concludes that an addition to the amount of water consumed will temporarily increase the excretion of nitrogen, but that such an increase is not permanent, and that the extra nitrogen washed out by the water would have been excreted normally, only somewhat later.

Neumann made a series of experiments of which he, himself, was the subject. These experiments continued for twenty-four days and were divided into five periods. In a preliminary period of four days he consumed a uniform diet and drank normal quantities of water. On the first day

of the second period 3 litres of water were added to the normal diet and the nitrogen excretion was raised from 12.09 grams to 15.990 grams. On the three following days, notwithstanding the daily consumption of at least 3 litres of water, the excretion of nitrogen gradually fell and an excretion of 12.2 grams was noted on the third day. During the third period Neumann investigated the influence of the withdrawal of water. Upon decreasing the amount of water from 3360 grams to 600 grams he secured a decrease of 2.4 grams in the nitrogen excretion. At this point, by increasing the amount of water ingested by 250 grams, an increase of 0.47 gram in the nitrogen excretion was noted, while a further addition of 50 grams to the amount of water consumed caused a further increase of 1.14 grams in the quantity of nitrogen excreted. In the following period of nine days Neumann investigated the influence of the consumption of large amounts of water. The first day an increase of 4.94 grams in the nitrogen excretion occurred as the result of an increase of 2365 grams in the amount of water taken, whereas after a like water ingestion on the day following, the excretion of nitrogen fell to 13.7 grams. During the next seven days the output of nitrogen was maintained at a somewhat lower level and the period was brought to a close on the ninth day with an excretion of 11.0 grams. The fifth and final period was devoted to the study of decreased amounts of water and similar results to those obtained in the third period were secured.

The study of the influence of an increase in the quantity of water consumed by diseased subjects has been the topic of a rather small number of investigations. Matzkevich,[33] in eight series of experiments of from sixteen to twenty-two days in duration, observed the influence of copious water drinking upon the assimilation and metabolism of nitrogen in typhoid-fever patients. From 2 to 3 litres of water were given daily. The author concludes that the assimilation of proteid was increased under the influence of copious water drinking, the increase being the most marked at the time of the highest temperature and decreasing during convalescence. The metabolism of nitrogen in 3 cases was least during the period of copious water drinking and greatest in the following period. In general, however, an increase in the metabolism of nitrogen was observed. The patients decreased more or less uniformly in weight. The author observed that drinking large amounts of water exerted no appreciable influence upon the pulse, respiration, or body temperature.

The object of Gruzdiev[34] in his experiments upon patients with acute fever was to compare the influence of copious and moderate water drinking upon the metabolism and assimilation of nitrogen, upon the blood pressure, and upon the excretions of the skin and lungs. The author describes eight metabolism experiments, each continuing for ten days, during the first portion of which large volumes of water were daily ingested and the last part of the period being devoted to the study of the ingestion of smaller volumes of water. The greatest quantity of water taken was 18 litres during a period of five days. This author claims that in febrile diseases the consumption of large volumes of water increases the metabolism of nitrogen. He further claims that an improved assimilation of nitrogen also occurs, and that this is accompanied by an increased arterial tension and more copious excretion by the skin and lungs. In the opinion of this author it is advisable for fever patients to consume large quantities of water, and he maintains that within reasonable bounds the physician in charge should insist upon copious water drinking.

Investigations by Dubelir,[35] Seegen,[36] and Fränkel[37] afford the conclusion that an increase in the amount of water ingested produces no increase in the excretion of nitrogen. The experiments of Dubelir were made upon a small male dog. The experimental plan included a period of three days in which a uniform diet was fed, followed by a period of similar length during which an addition of 300 c.c. of water was made to the diet daily. The experiment ended with a single day under the original normal conditions. The author is of the opinion that we should not be premature in asserting that an increase in the volume of urine after increased water ingestion is necessarily accompanied by an increased nitrogen excretion. His results seem to indicate, that with a daily addition of 300 c.c. to the amount of water ingested by a small dog, the nitrogen excretion may remain entirely unchanged, although the volume of the urine is increased.

Seegen, with a dog as subject, made an experiment fifty-six days in length. The daily volume of water consumed by the animal varied between 500 c.c. and 1800 c.c. The author concludes that the elimination of water by the kidneys appears to exercise no very appreciable effect upon the nitrogen excretion. The average nitrogen excretion from the daily diet of 1200 grams of meat was 41 grams, and this amount was excreted alike on days of large and small water ingestion. The period of greatest nitrogen excretion, strangely enough, was the period during which the least amount of urine was excreted. Seegen found the excretion of water by the lungs and skin to be uninfluenced by the drinking of large amounts of water, and claims the most copious perspiration to have occurred upon the day of the smallest water ingestion. Fränkel, by allowing a fasting dog 1210 grams of water at one time, noticed no effect in the excretion of urea.

Karchagin[38] made several experiments upon the influence of diminished water drinking upon the metabolism and assimilation of nitrogen in healthy persons. He used medical students as subjects. His experiments were divided into three periods of five days each. In the first and third periods the subjects were allowed a normal amount of water, and in the second period the amount was much decreased. Karchagin found when the water ingestion of a normal sub-

ject was diminished that the body weight fell, the volume of the urine decreased, and its specific gravity increased. He also concluded that the assimilation of nitrogen was somewhat improved while the metabolism of nitrogen was decreased to a slight degree. During the period of diminished water ingestion the subject did not feel as well as usual. On returning to the normal water ingestion during the third period, the body weight was found to increase, in some cases the increase being above normal.

Roux[39] in a single experiment secured data indicating a decrease in the excretion of urea accompanying copious water ingestion. During three days with an average ingestion of 925 grams of water he secured an average excretion of 32.4 grams of urea. This period was followed by a single day in which 2515 grams of water was ingested, and notwithstanding this large addition to the quantity of water ingested the daily urea output fell to 31.3 grams.

In addition to the investigators already mentioned, Speck,[40] Gley and Richet,[41] J. W. Paton,[42] Landauer,[43] Straub,[44] and Von Noorden[45] have given us points of varying interest regarding the effect of the ingestion of a large volume of water.

II. PURPOSE OF THE EXPERIMENTS.

Notwithstanding the fact that a large number of investigations have been made upon the influence of copious water drinking, yet nowhere in the literature, so far as we are aware, is there recorded the data from a carefully conducted series of experiments of this sort upon human subjects, having for its object the study of the course of the nitrogen, sulphate, and phosphate eliminations. The greater number of the experiments along this line were concerned solely with the excretion of nitrogen by the urine and in many instances the daily excretion of nitrogen was calculated from the urea content of the urine, a determination frequently made by methods now believed to be inaccurate.* Coupled with this inaccuracy we find in a large percentage of the experiments that no analyses of food or feces were made and no attempt made to get the subject into a condition of nitrogen equilibrium before commencing the experiment proper. In the absence of such necessary controls as those mentioned, metabolism work of this nature has very little practical value. Under such conditions the investigator's conclusions must be drawn solely from the data relating to the nitrogen content of the urine—data calculated upon the basis of unreliable analytical results.

Still other investigators used accurate methods for the direct determination of the nitrogen excretion by the urine and were very careful to get their subjects into a condition of approximate nitrogen equilibrium in a preliminary period by the use of a constant diet, but entirely neglected to make analyses of the feces. Obviously the data from such experiments do not permit of the drawing of any accurate conclusions regarding the relation existing between the income and outgo of nitrogen during any specified period, and therefore the preparation of a nitrogen balance is impossible.

In the experiments we are about to report the subjects* were placed on a constant diet, and by means of a preliminary period of sufficient length brought to a condition of approximate nitrogen, sulphur, and phosphorus equilibrium. At this point the regular constant diet was supplemented during a period of two days by a large volume of water taken daily at stated intervals. Immediately following this period of increased ingestion of water came a second period during which the original normal constant diet was again maintained.

The urine and feces were collected, the former in twenty-four-hour samples, the latter in period samples, and the content of nitrogen, sulphur, and phosphorus carefully determined by reliable methods.† The food was also subjected to careful analysis. By this method accurate data regarding the income and outgo of nitrogen, sulphur, and phosphorus were obtained and the drawing of definite conclusions made possible.

III. DESCRIPTION OF EXPERIMENT I.

Subject and Daily Schedule. The subject of this experiment was a young man twenty-nine years of age and weighing 61.51 kg.

The daily schedule for the preliminary and final periods of the experiment was as follows:

8.55 A.M., body weight determined.
9.00 A.M., breakfast and 100 c.c. water taken.
11.00 A.M., 100 c.c. water taken.
1.00 P.M., lunch.
3.30 P.M., 100 c.c. water taken.
6.00 P.M., dinner.
8.00 P.M., 100 c.c. water taken.
10.00 P.M., 100 c.c. water taken.

On the days of the increased water ingestion 4500 c.c. of water was added daily to the constant diet, this additional volume of water being given at the following hours:

11.00 A.M., 1000 c.c.
12.00 M., 1000 c.c.
3.30 P.M., 1000 c.c.
8.00 P.M., 1000 c.c.
10.00 P.M., 500 c.c.

Diet. The articles of diet were butter, wheat-flour crackers, and whole milk (see Table A), 75 grams of butter, 330 grams of crackers, and 1800 grams of whole milk constituting

* Ryan and Marshall. University of Pennsylvania Medical Bulletin, 1905, vol. xvii. p. 398.

* The author wishes to thank Dr. J. S. Chamberlain and Mr. A. E. Roberts for their kindness in acting as subjects during a part of the investigation.

† Methods of Analysis, p. 12.

the daily dietary. These were fed in constant amount from day to day in the form of three absolutely identical meals taken at 9 A.M., 1 P.M., and 6 P.M. respectively. Each meal therefore, consisted of 25 grams of butter, 110 grams of crackers, and 660 grams of whole milk.

Collection of Urine and Feces. The experimental day extended from 9 A.M. to 9 A.M. Just previous to the beginning of the day the urine was collected and added to the urine sample of the previous day. If possible the subject also defecated and then immediately determined his body weight. This schedule being carefully followed daily, it is obvious that each day was begun with the organism in very similar condition.

As has already been stated, the feces was collected in period samples. To secure satisfactory differentiation of the feces of one period from that of the following period, a gelatin capsule containing 0.2 gram of charcoal was taken just before breakfast of the day upon which the second period began. This formed a more or less regular black mass in the fecal matter and rendered the separation of the feces of the period preceding the taking of the charcoal, from the feces of the period following the taking of the charcoal, comparatively simple.

Methods of Analysis. The determinations of P_2O_5 were made by the fusion method. The method as used in the analysis of the foods and feces was as follows: 10 grams of sodium hydroxide and 2 grams of potassium nitrate were weighed into a silver crucible, fused and cooled. A weighed amount of the material under examination was now transferred to the crucible and gentle heat applied until the fused mass was clear. The mixture was then cooled, transferred to a casserole by means of hot water, acidified slightly with nitric acid, and evaporated to dryness on a water bath. The residue was moistened with a few drops of dilute nitric acid, dissolved in hot water, and transferred to a beaker. An equal volume of molybdic solution was now added and the mixture kept at 40° C. for twenty-four hours. The precipitate was then filtered off, washed with dilute molybdic solution, and dissolved in dilute ammonia. Dilute hydrochloric acid was now added to the filtrate, care being taken to leave the solution distinctly ammoniacal. Magnesia mixture (10 to 15 c.c.) was now added, and after stirring thoroughly and making strongly ammoniacal with concentrated ammonia, the solution was allowed to stand in a cool place for twenty-four hours. The precipitate was then filtered off, washed free from chlorine with dilute ammonia, and dried, incinerated, and weighed in the usual manner.

In the determination of P_2O_5 in the urine the following modification of the above method was used: 25 c.c. of urine was placed in the silver crucible and evaporated to dryness on a water bath. 10 grams of NaOH and 2 grams of KNO_3 were now added to the residue and the whole mass fused until all organic matter had disappeared and the fused mixture was clear. From this point the procedure was the same as for the determination of P_2O_5 in foods and feces.

The fusion method was also used for the determination of SO_3. In the analysis of the foods and feces the method up to the point of acidification and evaporation to dryness was the same as for the determination of P_2O_5 given above, and from that point the procedure was as follows: acidified slightly with HCl and evaporated to dryness on a water bath. The residue was moistened with a few drops of dilute HCl and brought into solution with hot water. The solution was now filtered, heated to boiling, and precipitated by barium chloride. The precipitate of barium sulphate was allowed to stand for twenty-four hours, then filtered off, and washed free from chlorine. It was then dried, incinerated, and weighed in the usual manner.

In the determination of SO_3 in the urine, the preliminary procedure was the same as that given above in the modification of the method for the determination of P_2O_5.

Nitrogen was determined by the Kjeldahl method, and the determinations of fat were made by ethyl-ether extractions.

IV. Discussion of Results (Experiment I.).

Excretion of Nitrogen. The nitrogen content of the urine for the second day of the preliminary period was 11.10 grams, and for the third day was 11.03 grams. The elimination of nitrogen by the urine being so very uniform for these two days, thus signifying that a satisfactory plane had been reached and that nitrogen equilibrium was fairly well established, on the following day, the fourth of the experiment, 1500 c.c. of water was added to the diet. The effect of this large addition to the amount of water taken was seen immediately, not only in the increased volume of urine having a very low specific gravity, but also in the marked increase in the nitrogen excretion for the day. This large amount of water was taken, as we have seen, when the body was in a condition of approximate nitrogen equilibrium and excreting daily an average of 11.065 grams of nitrogen by the urine. By an examination of Table B we see that this average excretion of nitrogen for the preliminary period was greatly increased by the drinking of 1500 c.c. of water additional and that the first day of the water period showed an excretion of 12.48 grams of nitrogen by the urine, an increase of 1.415 grams or 12.8 per cent., above the average elimination of the preliminary period. The excretion of nitrogen by the urine on the second day of the water period, while not so great as that of the first day, was still greatly in excess of the average normal output of the preliminary period. Here, with the addition of 1500 c.c. of water to the constant diet, we obtained an excretion of 11.82 grams of nitrogen, this total being 0.66 gram less than the elimination during the first day of the copious water drinking, but at the same time being 0.755

gram or 6.8 per cent., above the average daily excretion for the preliminary period. Hence, by referring to the data, we note that the influence of the addition of 9000 c.c. of water to the constant diet, during a period of forty-eight hours, was to cause an average daily increase of 1.085 grams in the excretion of nitrogen by the urine, or a total increase of 2.17 grams of nitrogen for the forty-eight-hour period.

On the sixth day of the experiment the final period of the investigation was begun. The diet of this day, as well as that of the three succeeding days, was the same constant diet as that fed during the preliminary period. This constant diet, which previous to the water period had given an average daily excretion of 11.065 grams of nitrogen by the urine, on this first day after the water period gave an excretion of 10.91 grams of nitrogen. Although slightly lower than the average daily excretion of the preliminary period, it was, on the whole, fairly comparable. The seventh day showed an elimination of 11.73 grams, which was 0.665 gram above the average daily excretion of the preliminary period. On the two following days the excretion of nitrogen was 11.17 grams and 11.01 grams respectively, thus indicating very clearly that the original condition of nitrogen equilibrium, which existed before the ingestion of the large volume of water, had been re-established. Therefore, the total effect upon the excretion of nitrogen by the urine, of the addition of 9000 c.c. of water to the diet during a period of forty-eight hours, is measured by taking into consideration all the daily excretions of nitrogen from the first day of the water period until the condition of nitrogen equilibrium was again established upon the eighth day. By referring to Table B we see that the average daily increase in the excretion of nitrogen by the urine during those four days was 0.67 gram, or a total of 2.68 grams for the ninety-six hours.

Thus, in the case of Subject 1, an addition of 9000 c.c. of water to a constant diet, after a condition of nitrogen equilibrium had been established, caused an increase of 2.68 grams in the excretion of nitrogen by the urine, the greatest increase being one of 1.415 grams, which occurred on the first day after the ingestion of 4500 c.c. of water, and the increase of 2.68 grams being distributed over a period of four days.

Excretion of SO_3. By referring to Table B we see that the average daily excretion of SO_3, for the days of the preliminary period when the organism had reached nitrogen equilibrium, was 1.685 grams. Upon examination of Table D we note that there was at this time a condition of praetically exact SO_3 equilibrium, the average daily balance being —0.04 gram of SO_3 for the two days. When the large volume of water was taken upon the fourth day we observe that an immediate rise in the amount of SO_3 excreted by the urine occurred, the total excretion for the day being 1.95 grams, or an increase of 0.265 gram above the average output of the normal preliminary period. The elimination of SO_3 for the second day of the water period was 1.88 grams, or an increase of 0.195 gram above the normal elimination. The excretion for the two days following the water period remained high, and following this upon the eighth day of the experiment the condition of SO_3 equilibrium was again established. As in the case of the nitrogen elimination, the total influence upon the elimination of SO_3 of the ingestion of the water may be measured only by taking into consideration the data of the excretions from the beginning of the water period to the time when SO_3 equilibrium was re-established. Calculating upon this basis, we find that the average normal output of SO_3 observed during the preliminary period, upon the constant diet, was increased by the water ingestion on an average 0.195 gram daily for a period of four days, the total increase being 0.77 gram for the four-day period. The excretion of SO_3 followed that of nitrogen, as measured in twenty-four-hour periods, in beginning its increased elimination upon the day of increased water ingestion and also in regaining its original equilibrium plane at the expiration of the second day after the close of the water period. The excretion of SO_3 differed from that of nitrogen in the fact that the increase in SO_3 on the first day of the copious water drinking was 15.6 per cent. above the normal, whereas the increase in nitrogen was but 12.8 per cent. The most striking contrast between the course of the two excretions, however, was seen in the fact that the total increase in the excretion of nitrogen, due to the influence of the water, was 6.0 per cent. above the normal, whereas the total increase in the excretion of SO_3 was 11.4 per cent. above the normal output of the preliminary period.

The total effect upon the SO_3 excretion of drinking 9000 c.c. of water during a period of forty-eight hours after the organism had reached practically exact SO_3 equilibrium, was to increase the excretion of SO_3 to the extent of 0.77 gram or 11.4 per cent. above the normal, in a period of four days, the greatest increase being one of 15.6 per cent., which occurred on the first day of the increased water ingestion, and was due primarily to the addition of 4500 c.c. of water to the constant diet.

Excretion of P_2O_5. The average daily excretion of P_2O_5 for the days preliminary to the water period was 2.34 grams. Immediately upon the ingestion of 4500 c.c. of water upon the first day of the water period, this average was increased by 0.22 gram or 9.4 per cent., the total elimination for the day being 2.56 grams. The maximum P_2O_5 excretion occurred upon the next day, the second day of the water period. On this day an excretion of 2.74 grams of P_2O_5 was registered, this being an increase of 0.40 gram or 17.1 per cent., above normal. Contrary to the course of the nitrogen and SO_3 excretions the excretion of P_2O_5 regained its normal plane of approximate P_2O_5 equilibrium in three days instead of four, as in the former cases. The course of the P_2O_5 excretion also differed from that of nitro-

gen and SO_3 in the fact that in the case of P_2O_5 we observed the greatest increase above normal to occur on the second day of the copious water drinking, whereas in the case of nitrogen and SO_3 the greatest increase occurred on the first day of the copious water drinking.

The total influence exerted upon the excretion of P_2O_5 by the urine, through the agency of 9000 c.c. of water ingested during a period of forty-eight hours, was to increase the excretion 0.77 gram or 10.9 per cent., above normal, the increase extending over a period of three days from the time of the initial increase in the ingested water and being greatest upon the second day.

V. Income and Outgo (Experiment I.).

Income and Outgo of Nitrogen. The income of nitrogen was of course represented by the nitrogen content of the articles of diet, while the outgo of nitrogen was represented by the nitrogen content of the urine and feces. Data for the income and outgo of nitrogen are given in tabular form in Table C. From the food analyses given in Table A we see that 12.84 grams of nitrogen was daily ingested in the diet, this diet being controlled so that the ingested nitrogen was identical in amount from day to day. By referring to Table C it may be noted that the total excretion of nitrogen by the urine for the preliminary period was 22.13 grams, and the excretion of nitrogen by the feces was 2.95 grams, thus making a total excretion of 25.08 grams for the two days of the preliminary period. We may further see that the total nitrogen ingested in the food during this same period was 25.68 grams. Thus it is very evident that 0.6 gram more nitrogen was taken into the body in the form of food material than was excreted in the form of urine and feces. The organism had therefore gained 0.6 gram of nitrogen in the course of the preliminary period of two days, an average daily gain of 0.3 gram. While not in exact nitrogen equilibrium we considered that this condition of gaining but 0.3 gram of nitrogen daily was a satisfactory basis upon which to study the influence of copious water drinking, and therefore on the day following, 4500 c.c. of water was taken. The effect of this water ingestion, as we have observed elsewhere, was immediate and pronounced. The excretion of nitrogen by the urine and feces was so stimulated that instead of showing a gain of nitrogen to the organism, an actual loss of 1.687 grams was noted for the period of two days during which the copious water drinking continued, or an average loss of 0.844 gram daily. Following this period of high water ingestion, there came a final normal period of four days, in which the constant diet of the preliminary period was fed. During this period the organism reacted from the influence of the increased water ingestion and again showed a gain of nitrogen. The total gain for the four days was 1.972 grams, or an average daily gain of 0.493 gram. By thus re-establishing approximate nitrogen equilibrium, the organism was brought into practically the same condition as it was in at the time the large amount of water was added to the constant diet. The balance for the entire experiment showed a daily gain of but 0.11 gram of nitrogen.

Income and Outgo of SO_3. The daily SO_3 content of the food, as shown by the analyses in Table A, was 3.165 grams. During the preliminary period of two days, therefore, 6.33 grams of SO_3 was ingested, and during the same period, as may be seen by examining Table D, 3.37 grams of SO_3 was excreted by the urine and 3.04 grams of SO_3 was excreted by the feces. There was then a total excretion of 6.41 grams of SO_3 for the two days. Thus the very satisfactory condition of practically exact SO_3 equilibrium was secured by this preliminary period, the organism at the time of the initial ingestion of the large amount of water showing an average daily loss of but 0.04 gram of SO_3. The drinking of the 9000 c.c. of water during the period of two days increased the excretion of SO_3 as we have already seen, and caused the organism to show a loss of SO_3, aggregating 0.3 gram per day. The final normal period following the water period, showed a falling off in the amount of SO_3 excreted, and the balance, instead of showing a loss of SO_3 to the body, indicated an actual gain of 0.12 gram daily. This again, in so very nearly approaching a condition of actual equilibrium, made a very satisfactory closing point for the experiment. The total balance for the entire eight days showed a loss of but 0.09 gram of SO_3 per day.

Income and Outgo of P_2O_5. The daily ingestion of P_2O_5, as shown by the analyses of the foods (Table A), was 5.226 grams. Thus, during the preliminary period of two days 10.452 grams constituted the income of P_2O_5. During the same forty-eight hours, as shown in Table E, 4.68 grams of P_2O_5 was excreted by the urine and 4.78 grams was excreted by the feces, making a total outgo of 9.46 grams. Therefore, at the beginning of the water period, the organism was gaining 0.496 gram of P_2O_5 daily. The two days of copious water drinking, during which 9000 c.c. above the normal amount of water was consumed, served to increase the excretion of P_2O_5 by the urine so that the total excretion of P_2O_5 by the urine and the feces, for the period of two days, was 10.02 grams. This caused the gain of P_2O_5 by the organism to be decreased somewhat and showed an average gain of 0.216 gram of P_2O_5 daily. During the final period of four days, when the original constant diet was fed, the normal conditions again obtained and a daily gain by the organism, of 0.588 gram of P_2O_5, was registered. The total balance for the entire experiment showed a gain of 0.472 gram of P_2O_5 daily.

The excretion of P_2O_5 by the feces is very striking, as may be seen by an examination of Table E or Table F. Of the total elimination of P_2O_5 for the preliminary period, 50.5 per cent. was eliminated by the feces. During the water

period the somewhat smaller amount of 47.2 per cent. was thus excreted, whereas during the final period the output by the feces was 50.2 per cent. of the total output.

VI. DESCRIPTION OF EXPERIMENT II.

SUBJECTS, DAILY SCHEDULE, DIET, ETC. The subjects of this experiment were two young men aged twenty-six and twenty-eight years, respectively. The daily schedule was as follows:

6.30 A.M., breakfast.
9.30 A.M., 300 c.c. water taken.
12.30 P.M., lunch.
3.30 P.M., 300 c.c. water taken.
6.30 P.M., dinner.
9.30 P.M., 300 c.c. water taken.

Upon the days of increased water ingestion, 4000 c.c. of water, an addition of 3100 c.c. to the constant diet, was taken daily as follows:

6.30 A.M. to 12.30 P.M., 1500 c.c.
12.30 P.M. to 6.30 P.M., 1500 c.c.
6.30 P.M. to 9.30 P.M., 1000 c.c.

The diet (Table G) was qualitatively the same as that of Experiment I.—*i. e.*, crackers, butter, and whole milk. In this experiment, however, 1650 grams of whole milk, 60 grams of butter, and 300 grams of crackers constituted the daily diet. It was eaten at three similar meals taken at the hours indicated in the above schedule.

The methods for the collection of urine and feces were the same as in Experiment I.

VII. DISCUSSION OF RESULTS (EXPERIMENT II.).

EXCRETION OF NITROGEN BY SUBJECT II. The average daily excretion of nitrogen by the urine by Subject II. during the three days of the preliminary period, as may be seen by referring to Table H, was 12.88 grams. On the fourth day, when the normal ingestion of water was increased by 3100 c.c., the total excretion of nitrogen for the day rose to 14.45 grams, and showed an increase of 1.57 grams or 12.2 per cent. above the normal for the twenty-four hours. On the second day of the increased water ingestion, the total amount of nitrogen excreted by the urine showed a remarkable drop and registered only 12.43 grams for the day. This was a decrease of 2.02 grams from the excretion of the previous day, and was also less than the average daily excretion of the preliminary period. When we remember that the constant diet was supplemented on this day by 3100 c.c. of water, this drop of over 2 grams below the total excretion of the previous day on the same water ingestion is rather impressive. On the normal day, following the water period, this downward tendency in the course of the nitrogen excretion was still apparent and the total excretion of nitrogen by the urine for that day was but 10.32 grams.

In the case of Subject II. we therefore found that 3100 c.c. of water added to the diet, after the organism had been brought to a condition of approximate nitrogenous equilibrium, caused an increase on the first day of 1.57 grams or 12.2 per cent., in the excretion of nitrogen by the urine, but that this initial increase was more than compensated by the exceptionally low excretions of the two following days.

EXCRETION OF NITROGEN BY SUBJECT III. The average daily normal excretion of nitrogen by the urine for this subject during the preliminary period of three days was 11.81 grams. Upon the first day of the water period, when 3100 c.c. of water was added to the diet for the day, the total excretion for the twenty-four hours was increased to 12.93 grams, this being an actual increase of 1.12 grams or 9.5 per cent., above normal. The excretion for the second day of the water period also remained high and showed an increase of 0.78 gram or 6.6 per cent., above the normal excretion of the preliminary period. The single day of the final normal period showed a satisfactory return to the normal excretion. In thus returning to the normal rate, the course of the excretion of nitrogen by Subject III. very closely resembled that by Subject I. in Experiment I., but was entirely different from the course of the excretion by Subject II. in Experiment II.

In the case of Subject III. the influence of the water was to increase the excretion of nitrogen by the urine 1.9 grams, or 8.0 per cent., in a period of forty-eight hours, this increase being followed by an immediate return to normal conditions, as regarded the course of the nitrogen excretion by the urine. We may therefore say, that in this subject a total increase of 6200 c.c. in the amount of water ingested in forty-eight hours, after the course of the nitrogen excretion by the urine had become fairly constant, was to cause an immediate increase in the excretion of nitrogen on the first day of 1.12 grams or 9.5 per cent., above normal, and a further increase on the second day of 0.78 gram or 6.6 per cent., above normal, these two days of increased nitrogen excretion being followed by a final day on a normal diet in which the course of the nitrogen excretion again assumed the normal rate.

EXCRETION OF SO_3 BY SUBJECT II. The average daily excretion of SO_3 by the urine by this subject for the two days immediately preceding the water period was 1.966 grams. On the first day of the increased water ingestion the excretion remained practically unchanged (1.95 grams), but on the second day the somewhat lower excretion of 1.842 grams was registered. This was an actual decrease of 0.124 gram or 6.3 per cent. Upon the final day, when the normal conditions which were in force during the preliminary period again existed, the excretion fell still farther and an output of 1.787 grams was recorded, this being a decrease of 0.179 gram or 9.1 per cent., below normal.

The influence upon the course of the SO_3 excretion by the urine, of the taking of 6200 c.c. of water during a period of forty-eight hours, was to cause a decrease of 0.140 gram or 3.5 per cent., for the period.

Excretion of SO_3 by Subject III. The data for the two days previous to the ingestion of the large amount of water showed an average daily excretion of 1.789 grams of SO_3. Upon the first day of the water period the course of the SO_3 excretion was subjected to a decided depression, the total excretion being but 1.48 grams, a decrease of 0.309 gram or 20.9 per cent., below the normal daily excretion of the preliminary period. On the second day of the water period the excretion recovered slightly from the depression of the day before, but still showed a decrease of 0.258 gram or 14.4 per cent., below the normal output. The final day on the normal diet, the excretion of SO_3 showed a marked recovery, the total excretion for the day being 1.775 grams, which was in very close agreement with the average daily excretion of the preliminary period. With Subject III. the effect upon the excretion of SO_3 by the urine, of 6200 c.c. of water taken during a period of forty-eight hours, was to decrease the excretion 0.567 gram or 15.8 per cent., below normal, the decrease being more pronounced on the first day. Following this pronounced decrease the excretion recovered rapidly and showed a normal excretion on the final day of the experiment.

Excretion of P_2O_5 by Subject II. By referring to Table II it will be seen that the average daily excretion of P_2O_5 by the urine for the three-day preliminary period was 2.557 grams. It will be further noted that the effect of the 3100 c.c. of water taken on the first day of the water period was to cause a very slight increase in the excretion, the total output for the day being 2.568 grams. On the second day of the water period, however, a much larger total excretion was recorded, the amount for the twenty-four hours being 2.653 grams. The final day of the experiment on the normal constant diet gave the subnormal excretion of 1.840 grams. In reaching the point of maximum excretion on the second day of the increased water ingestion, the course of the P_2O_5 excretion with this subject was the same as that found in Experiment I.

The influence of the 6200 c.c. of water, taken during a period of forty-eight hours, was therefore to cause an increase of 0.107 gram or 2 per cent., in the excretion of P_2O_5 by the urine, the increase beginning immediately and reaching its maximum output on the second day.

Excretion of P_2O_5 by Subject III. The excretion of P_2O_5 by Subject III. followed practically the same course as that of Subject II. The average daily excretion for the preliminary period was 2.241 grams, and this normal output was increased by the consumption of the excessive amount of water, causing a total output of 2.479 grams on the first day and one of 2.7 grams on the second day. The increase in the excretion of P_2O_5 due to the water was, therefore, 0.238 gram or 10.6 per cent., on the first day and 0.459 gram or 20.5 per cent., on the second day. The aggregate increase for the two days of the water period was 0.697 gram or 15.5 per cent. In accord with the data for the excretion of P_2O_5 by Subject II., the final day of the experiment, when the original constant diet was resumed, gave a subnormal excretion of P_2O_5 by the urine.

The effect of the 6200 c.c. of water added to the diet of Subject III., after a condition of approximate P_2O_5 equilibrium had been reached, was to cause an increase of 10.6 per cent. on the first day and the maximum increase of 20.5 per cent. on the second day.

VIII. Income and Outgo (Experiment II.).

Income and Outgo of Nitrogen (Subject II.). By referring to Table I we learn that the total amount of nitrogen ingested daily in the constant diet was 14.29 grams, or a total of 12.87 grams for the preliminary period of three days. Of this amount 38.762 grams was excreted by the urine and 1.554 grams by the feces during that period. Thus the organism was gaining nitrogen at the rate of 0.851 gram per day at the time the study of the influence of copious water drinking was started. As is shown by the data for the water period, the ingestion of 6200 c.c. of water additional in the two days caused an immediate increase in the excretion of nitrogen and a consequent loss of nitrogen to the organism. On an ingestion of 28.58 grams of nitrogen the subject excreted 26.88 grams by the urine and 1.56 grams by the feces, thus showing an average daily gain by the body of but 0.09 gram of nitrogen. In the final period, when the original normal diet was again fed and the water reduced to the normal amount, there was a striking depression in the excretion of nitrogen by the urine, causing a gain of 3.18 grams of nitrogen by the organism in twenty-four hours.

Income and Outgo of Nitrogen (Subject III.). As we have seen in our discussion of the nitrogen excretion by Subject III., the course of the excretion ran very fairly constant during the three days preliminary to the water period. Notwithstanding this constancy in the amount of nitrogen excreted by the urine from day to day, there was a comparatively large gain of nitrogen to the body during these days, due to the fact that the excretion was on a rather low plane relative to the income of nitrogen. Therefore during this preliminary period, although the daily excretions were very uniform, there was an average daily gain of 1.852 grams of nitrogen to the body. In the water period the customary stimulation of the excretion of nitrogen by the urine was noted, with the result that the large average daily gain of the preliminary period was reduced to a gain of but 0.86 gram per day. The final day of the experiment, when the constant diet was again fed, showed a return to the

original low plane of nitrogen excretion and a consequent gain of 1.730 grams of nitrogen by the organism.

IX. DESCRIPTION OF EXPERIMENT III.

Subjects, Daily Schedule, Diet, etc. The subjects of this experiment were two young men, Subject IV. being twenty-six years of age and subject V. being one year younger. At the beginning of the experiment Subject IV. weighed 62.8 kg. and Subject V. weighed 61.4 kg., while at the end of the experiment their weights were 63.6 kg. and 61.0 kg. respectively. Thus Subject IV. gained 0.8 kg. during the four days he was under examination and Subject V. lost 0.4 kg. during the six days of his test. The daily schedule was similar to that of Experiment II. The schedule follows:

6.30 A.M., breakfast.
9.30 A.M., 300 c.c. water taken.
12.30 P.M., lunch.
3.30 P.M., 300 c.c. water taken.
6.30 P.M., dinner.
9.30 P.M., 300 c.c. water taken.

Upon the days of increased water ingestion, instead of drinking 300 c.c. of water three times each day at intervals of six hours beginning at 9.30 A.M., as shown by the above schedule, the subjects were given 500 c.c. of water every two hours from 7.30 A.M. until 9.30 P.M. The total water consumption for the day was, therefore, 4000 c.c., an addition of 3100 c.c. to the normal amount. Identically the same diet (Table J) was fed in this experiment as was used in Experiment II.—*i. e.*, a constant diet containing daily 1650 grams of whole milk, 300 grams of crackers, and 60 grams of butter. This was fed at three similar meals taken at the hours mentioned above. The customary methods for the collection of urine and feces were in force during this experiment.

X. DISCUSSION OF RESULTS (EXPERIMENT III.).

Excretion of Nitrogen by Subject IV. The average daily output of nitrogen by the urine for the two days of the preliminary period was, according to the data given in Table K, 14.03 grams. Upon the ingestion of 3100 c.c. of water, however, on the third day of the experiment, this normal output was increased to 14.86 grams, an increase of 0.83 gram or 5.9 per cent., above the normal. The total excretion for the next twenty-four hours upon the increased water ingestion fell somewhat below this maximum excretion of the first day of the water period, but still remained very considerably higher than the normal excretion. The excretion of nitrogen by the urine for this day was 14.41 grams, an increase of 0.38 gram or 2.7 per cent., above the normal excretion. The total increase in the excretion of nitrogen for the two days of the water period was, therefore, 1.21 grams or 4.3 per cent., above the normal. Unfortunately, the conditions were not such as to allow a final normal period with this subject.

In the case of Subject IV. the drinking of 6200 c.c. of water additional during a period of forty-eight hours, was instrumental in increasing the excretion of nitrogen by the urine 1.21 grams or 4.3 per cent., in that period, the maximum increase being one of 0.83 gram or 5.9 per cent., which occurred during the first twenty-four hours.

Excretion of Nitrogen by Subject V. The data for the excretion of nitrogen by this subject indicates that the subject was running on a somewhat lower nitrogen level than Subject IV., although each was receiving the same amount of nitrogen in the food. The average daily excretion of nitrogen by the urine by Subject V. was therefore 13.37 grams for the two days of the preliminary period. This was 0.66 grams per day lower than the normal output of Subject IV. The usual increase of 3100 c.c. in the amount of water ingested caused an excretion of 14.43 grams of nitrogen by the urine upon the first day of the water period. This was an increase of 1.06 grams or 7.9 per cent., above the normal. In complete agreement with the course of the nitrogen excretion of Subject IV., the excretion of the second day of the water period, while still considerably above the excretion of the normal period, was depressed somewhat from the decided increase of the first day of the water period. The excretion for the second day was 13.95 grams, an increase of 0.58 gram or 4.3 per cent., above the normal.

By calculating upon the basis of the increased excretion of each of the two days of the water period, we see that the total effect of the 6200 c.c. of water was to increase the output of nitrogen by the urine 1.64 grams or 6.1 per cent., in the forty-eight-hour period. A final period of two days, under normal conditions, caused the excretion of nitrogen by the urine to undergo a decided depression from the abnormally large excretion due to the copious water ingestion. The last day of this normal period gave an excretion of 13.32 grams of nitrogen by the urine, this being practically the same as the average normal excretion (13.37) of the preliminary days. The drinking of 6200 c.c. of water additional during a period of forty-eight hours was therefore the means of causing a decided increase in the excretion of nitrogen by the urine. This increase began immediately and continued for seventy-two hours, during which time the normal excretion of nitrogen by the urine was increased by 1.97 grams or 4.9 per cent.

Excretion of SO_3 by Subject IV. The average daily excretion of SO_3 by the urine for the preliminary period was 2.071 grams. The influence of the copious water drinking was shown, on the first day of the water period, by increasing the excretion for the day to 2.156 grams, this being an increase of 0.085 gram or 4.1 per cent. above the normal average daily excretion. On the second day of the increased

water ingestion, notwithstanding the fact that the same amount of water was ingested as on the first day of this period, the excretion of SO_3 by the urine was decreased perceptibly. The excretion for this day was 2.038 grams, a decrease of 0.033 gram or 1.6 per cent., below the normal average daily excretion. The total increase during the two days in which the quantity of water in the diet was increased was 0.052 gram or 1.2 per cent., above the normal. The course of the SO_3 excretion followed that of nitrogen, for this subject, in showing the maximum excretion on the first day of the increased water ingestion, but differed from the course of the nitrogen excretion in showing a subnormal excretion on the second day of the water period.

With this subject, then, an addition of 6200 c.c. of water to the diet caused a maximum increase of 0.085 gram or 4.1 per cent., in the excretion of SO_3 by the urine on the first day, and this was followed on the second day by an excretion slightly subnormal.

Excretion of SO_3 by Subject V. The normal average daily excretion of SO_3 during the two preliminary days was 2.039 grams. This was subjected to a decided increase under the influence of the 3100 c.c. of water ingested on the first day of the water period, the excretion for the twenty-four hours being 2.241 grams, an increase of 0.205 gram or 10 per cent., above the normal. On the second day of the water period the excretion of SO_3, while remaining above normal, was somewhat less than on the first day of the period. The excretion for the second day was 2.167 grams, an increase of 0.128 gram or 6.2 per cent., above the normal. The excretion underwent a gradual depression during the days of the final normal period, but did not quite reach the normal level at the expiration of the experiment.

The course of the SO_3 excretion followed that of nitrogen, for this subject, in showing the maximum excretion on the first day of the water period and in following this day of maximum excretion by daily excretions which were progressively less in amount; it differed from the nitrogen excretion in maintaining a level slightly above the normal level during the final period in which the original constant diet was fed. Taking into consideration the total SO_3 excretion from the beginning of the water period to the end of the experiment, we may say that the copious water drinking caused an increase of 0.423 gram or 5.2 per cent., in the excretion of SO_3 during a period of four days.

We may conclude from the data of this subject that the effect upon the excretion of SO_3 by the urine of 6200 c.c. of water ingested during a period of forty-eight hours was to cause a total increase of 0.423 gram or 5.2 per cent., in this excretion, the maximum output being one of 0.205 gram, or 10 per cent., which occurred on the initial day of the water period.

Excretion of P_2O_5 by Subject IV. The average daily excretion of P_2O_5 by the urine during the preliminary period was 2.925 grams. The drinking of 3100 c.c. of water on the first day of the water period caused an increase in the output of P_2O_5. The total excretion for the day was 3.061 grams, an increase of 0.136 gram or 4.7 per cent., above the normal. On the second day of the water period the excretion was still further increased, the total output for the day being 3.393 grams. This was an increase of 0.468 gram or 16 per cent., above the normal daily output. The course of the P_2O_5 excretion differed from that of nitrogen or SO_3, in this experiment, in showing the maximum excretion on the second day of the water ingestion instead of on the first. In showing this tendency to reach the point of maximum excretion on the second day of the water ingestion, the course of the P_2O_5 excretion for this subject agreed with the data from the other experiments.

The final effect, then, of the drinking of 6200 c.c. of water additional during the period of forty-eight hours, upon the excretion of P_2O_5 by the urine, was to cause an increase of 0.601 gram or 10.3 per cent., in the excretion, the maximum increase being one of 0.468 gram or 16 per cent., which occurred on the second day of the period.

Excretion of P_2O_5 by Subject V. The average daily excretion of P_2O_5 by the urine during the preliminary period of two days was 2.766 grams. Under the influence of the copious water drinking this normal output was increased to 2.883 grams upon the first day of the water period. This was an increase of 0.117 gram or 4.2 per cent., above the normal. On the second day of the period the maximum excretion of P_2O_5, for this subject, was recorded. This was an excretion of 3.002 grams, an increase of 0.236 gram or 8.5 per cent., above the normal excretion. During the final period on a normal diet, the excretion of P_2O_5 decreased decidedly, but failed to completely return to the normal level. The course of the P_2O_5 excretion differed from that of nitrogen or SO_3, for this subject, in showing the maximum excretion on the second day rather than on the first day of the increased water ingestion. As has already been indicated, this tendency for the P_2O_5 maximum excretion to occur so late, with reference to the maximum excretion of nitrogen and SO_3, was a uniform tendency exhibited throughout the series of experiments with each individual subject.

The effect upon the excretion of P_2O_5, of 6200 c.c. of water taken during a period of forty-eight hours, was to increase the excretion 0.467 gram or 1.2 per cent., the maximum excretion being one of 0.236 gram or 8.5 per cent., which occurred on the second day.

XI. Income and Outgo (Experiment III.).

Income and Outgo of Nitrogen (Subject IV.). By referring to Table I. it may be seen that 14.86 grams of nitrogen was ingested daily during the experiment. During the preliminary period 14.84 grams of nitrogen was excreted daily in the form of urine and feces. Thus the organism

was in practically absolute nitrogen equilibrium, as there was a daily gain to the body of but 0.02 gram of nitrogen. This made an exceptionally fine starting point for our study of the influence of copious water drinking. The nitrogen excretion during the water period of two days was 31.28 grams. The influence of the water, therefore, was to cause an increase in the excretion of nitrogen by the urine and feces and a consequent average daily loss of 0.78 gram of nitrogen to the organism.

Income and Outgo of Nitrogen (Subject V.). Owing to the fact that this subject was running on a somewhat lower plane of nitrogen elimination than subject IV., the preliminary period did not serve to produce such a close approximation to nitrogen equilibrium as was secured with that subject. The organism, in the case of Subject V., showed an average daily gain of 0.71 gram of nitrogen during the preliminary period. Although the starting points were not identical in the two instances, yet we notice from an examination of the data that the effect of the water was practically the same in the two cases as regards the increase produced in the excretion of nitrogen. In the case of Subject IV. the preliminary condition of +0.02 gram was changed by the water to —0.78 gram, whereas in the case of Subject V. the preliminary condition of +0.71 gram was changed to —0.005 gram by the same agency. During the final period of two days, during which the original constant diet was fed, the organism returned to practically the same condition that it was in before the large amount of water was added to the diet. In this period the body gained 0.63 gram of nitrogen daily, which compares favorably with the daily gain of 0.71 gram of the preliminary period.

Income and Outgo of SO_3 (Subject IV.). The amount of SO_3 ingested daily in the food, according to Table M, was 3.37 grams. Of this amount, during the preliminary period, an average of 2.941 grams was excreted daily by the urine and feces. There was therefore during this period a daily gain of 0.429 gram of SO_3 to the organism. During the water period the excretion of SO_3 by both the urine and the feces was stimulated somewhat, and this increased excretion was instrumental in lowering the daily gain of nitrogen to 0.323 gram.

Income and Outgo of SO_3 (Subject V.). Conditions regarding the income and outgo of SO_3 for this subject were very similar to those for Subject IV. Here upon the normal daily ingestion of 3.37 grams of SO_3, during the preliminary period, there was excreted a daily average of 2.999 grams by the urine and feces. Thus the body was gaining 0.37 gram of SO_3 daily, and in this the data compared favorably with the daily gain of 0.429 gram by Subject IV. Also in complete agreement with the result in the case of Subject IV. was the increased excretion of SO_3 during the period of high water ingestion. Under the influence of this large volume of water the daily gain of SO_3 to the body was decreased to 0.2 gram. During the final period upon the normal water ingestion the conditions observed in the preliminary period were restored, the excretion of SO_3 by the urine and feces was decreased, and the body consequently gained a larger amount of SO_3 daily. The average daily gain during this normal period was 0.381 gram, which compared very nicely with the average daily gain of 0.37 gram observed during the preliminary period.

Income and Outgo of P_2O_5 (Subject IV.). The daily income of P_2O_5, as may be seen by an examination of Table N, was 4.96 grams. During the preliminary period of two days, upon a total ingestion of 9.92 grams P_2O_5, 5.85 grams of P_2O_5 was excreted by the urine and 3.78 grams was excreted by the feces. Thus during this time the body was gaining 0.145 gram of P_2O_5 daily. In the water period, when 3100 c.c. of water was being daily added to the diet, the excretion of P_2O_5 by the urine and feces was markedly increased. Instead of gaining P_2O_5, the body was actually losing 0.462 gram daily, through the agency of the increased water ingestion.

Income and Outgo of P_2O_5 (Subject V.). Similar conditions relative to the income and outgo of P_2O_5 prevailed here as those noted above. During the preliminary normal period the organism was gaining 0.279 gram of P_2O_5. In the water period, however, owing to the increased excretion of P_2O_5, the body lost 0.0025 gram of P_2O_5. The final period, under normal conditions, saw a very satisfactory return to the original state and registered a gain of 0.207 gram of P_2O_5 daily, which compared very favorably with the daily gain of 0.279 gram observed during the preliminary period.

XII. Percentage of Ingested Water Excreted by the Urine.

In Table O is given, in tabular form, the data regarding the relation existing between the volume of fluid ingested daily and the total volume of the urine for the corresponding period. The percentage of ingested fluid recovered varied greatly in the different experiments as well as on different days of the same experiment. For instance, on the second day of Experiment II., Subject III. eliminated but 28.5 per cent. of the ingested fluid, whereas on the fifth day of Experiment I., Subject I. eliminated 90.6 per cent. of the ingested fluid. It will be noted, however, that the 28.5 per cent. was eliminated on a daily ingestion of 2300 c.c. of fluid, while the 90.6 per cent. was recovered on a daily consumption of 6400 c.c. of fluid. This same tendency for the larger percentage of the ingested fluid to be excreted on the days of copious water drinking was shown throughout the series of experiments. This was of course to be expected since the normal organism needs a certain amount of fluid for its normal processes, and any amount in excess would be rapidly and more or less completely eliminated.

XIII. GENERAL SUMMARY.

There are two views regarding the cause for the increased nitrogen excretion after the ingestion of large volumes of water. One is that it is due to an increased proteid catabolism, and the other that it is simply due to the washing out of the tissues of the urea previously formed, and which normal *flushing out* does not remove. Among the older investigators holding the former view are Bischoff, Genth, Becher, Mosler, and Bidder and Schmidt. In experiments by these men from 2 to 10 litres of water were given daily, and increases of from 10 per cent. to 35 per cent. in the nitrogen output were noted.

Voit and Forster, in later investigations, also showed an increased nitrogen excretion after copious water drinking. They worked on fasting dogs, and secured an increase of from 25 per cent. to 90 per cent. in the nitrogen excretion. Voit, after allowing his animal no water for three days, on the fourth day gave the beast 1957 c.c. of the fluid. This volume of water increased the urine output from 177 c.c. to 742 c.c. and the urea excretion from 16.7 grams to 21.3 grams. He says: "This increase is too great to be due to a simple flushing out." Forster, after fasting a dog for three days, introduced 3 litres of water into the dog's stomach and secured an increase from 182 c.c. to 2010 c.c. in the urine volume, and an increase from 12.5 grams to 22.9 grams in the urea output. Forster says it would seem incredible that so large an amount of urea could have been retained in the tissues and have been washed out at this time.

Munk did some work along the same lines with a dog under normal conditions of nutrition, and found a very slight increase in the nitrogen excretion. He holds the view that the increase is due simply to the removal from the tissues of urea previously formed.

Henneberg, in experiments upon oxen, after feeding 11 litres of water found an increase of but 7.2 per cent. in the nitrogen output; while Stohmann, using goats as subjects, on an ingestion of but 3 litres was successful in producing an increase of 14 per cent. in the nitrogen excretion. Frankel, while he increased the volume of water from 300 c.c. to 1700 c.c., found an average increase of only 9 per cent. in the nitrogen excretion. Thus we see that an increased ingestion of water does not always give a relatively large increase in the nitrogen output.

In harmony with the view enunciated above are the results secured by Seegen and by Roux. Seegen, upon doubling the water ingestion, found no perceptible increase in the urea excretion, while Roux noticed a decrease in the urea output after tripling the water ingestion.

The results of Meyer, who experimented upon dogs, and Oppenheim and Von Noorden, who experimented upon men, rather substantiate the theory that the increase in urea is a result of the washing out of the tissues. Meyer, after getting his dog into nitrogen equilibrium upon a meat diet, fed the animal 600 c.c. of water daily for sixteen days. On the first day an increase of 9 per cent. in the nitrogen excretion was noted, on the second day one of 4 per cent., and on the third day one of 2 per cent. On the remaining thirteen days there was no increase and the animal remained in nitrogen equilibrium. In two experiments Von Noorden reaches similar conclusions. Oppenheim found the nitrogen excretion to return to the normal four hours after increasing his water ingestion by 2 litres.

From an examination of the data offered by the different investigators it is apparent that, for the most part, those men who obtained the greatest increase in the excretion of nitrogen following the ingestion of large volumes of water, used *fasting* animals as subjects. It will be further seen that, in general, these investigators hold the belief that the increase they obtained was due to increased proteid catabolism, since the increase was considered by them too great to be accounted for by supposing it to be due to a flushing out of the tissues. Now it must be evident to all that we cannot conscientiously compare results obtained from experiments upon a fasting organism with those obtained from experiments upon an organism being maintained under conditions of normal nutrition. In the fasting organism it is obvious that the fluid, withdrawn from the tissues and excreted as urine, would not be sufficient to completely remove the urea as formed in the catabolism of tissue proteids. Under such a condition, therefore, urea would accumulate in the tissues in relatively large amount in a few days. Now cause such an organism to ingest a large volume of water, and it is evident that the urea output must be very largely increased at once, due primarily, we believe, to a washing out of this stored-up urea and, secondarily, to the effect of the water in stimulating proteid catabolism.

On the other hand, the conditions in a *normally fed* organism would be radically different. In this case the organism is ingesting a normal volume of water daily, thus preventing an excessive accumulation of urea in the tissues. Cause *such* an organism to ingest a large volume of water, in addition to the amount in the normal diet, and the result must naturally be quite different from that observed in the case of the fasting organism. There has been no large accumulation of urea in the tissues of the normally fed organism, due to the fact that the normal water ingestion has been sufficient to remove the bulk of the urea as formed. Some urea must escape immediate elimination, however, and this would be washed out by the copious water ingestion, and would serve to increase the nitrogen excretion for the day. But obviously the increase in the case of the normally fed animal must be decidedly less than the increase in the case of the fasting animal.

In our opinion, then, the data from the experiments upon fasting animals, instead of proving the truth of the theory that the increase in the nitrogen excretion, after copious

water drinking, is due principally to increased proteid catabolism, go rather to verify the theory that the increase noted under such conditions is due primarily to a flushing out of the tissues.

The data from our own experiments seem to indicate that the greater part of the increase in the nitrogen excretion which accompanies copious water drinking is probably due to the washing out of the tissues of urea previously formed, but which has not been removed in the normal processes. That a portion of the increase in the nitrogen excretion may also arise from a stimulation of proteid catabolism through the agency of the large volume of water ingested in a comparatively short time, also appears plausible. Any increase due to this second cause, however, we believe would be relatively slight. This increase would also probably begin somewhat later than the increase due to a flushing out of the tissues, and would continue for a longer period.

Upon glancing at the data for the excretion of nitrogen given in Tables B, H, and K it will be at once apparent that the above interpretation of the results is evidently the correct one. In every instance it will be noted that the greatest increase in the excretion of nitrogen occurred upon the first day of the water period, that the excretion of the second day of the water period was somewhat lower, although still above normal, and that following this, upon being fed the normal diet, the organism gradually returned to nitrogen equilibrium. This order of events was particularly well shown in Experiment I. with Subject I. According to our view, then, this initial large increase in the excretion of nitrogen by the urine was primarily due to the washing out of the tissues of urea already formed; the influence of the water in stimulating proteid catabolism was of secondary importance. Upon the second day of the copious water drinking, however, the increase in the nitrogen was dependent relatively less upon the flushing out process and more upon the stimulation of proteid catabolism, and therefore under these conditions the increase, as compared with the increase noted on the first day, was relatively small.

It will be noted that there was a general tendency for the excretion of SO_3 to run parallel with that of nitrogen.

The course of the P_2O_5 excretion was radically different from the course of the nitrogen or sulphur excretion. As has been said, the increase in the excretion of nitrogen occurred upon the *first* day of the water period in every instance, and the course of the excretion of SO_3 was fairly comparable. On the other hand, the maximum excretion of P_2O_5 occurred, in every experiment with absolute constancy, upon the *second* day of the water period. Now, it is very evident that neither of the views advanced above for the cause of the increase in the excretion of nitrogen can reasonably serve as a plausible explanation for the increase in the excretion of P_2O_5. This increase cannot be due to a washing out of the tissues, since it does not occur until the second day of the water period; and it certainly is not due to a stimulation of proteid catabolism, since the tissue proteids contain no phosphorus. As is well known, the phosphorus excretion arises from the catabolism of an entirely different form of material than that which gives rise to the nitrogen excretion. For the increase in the phosphorus excretion we must look primarily to the nucleins, lecithins, and other phosphorus-containing bodies.

Taking the data from our experiments into consideration there appears to us but one plausible explanation for the increase in the excretion of phosphorus after copious water drinking. We believe the increase in the excretion of phosphorus to have been due to the influence of the water in increasing cellular activity and in thus hastening the catabolism of phosphorus-containing bodies, particularly nucleins and lecithins. It is evident that an increase due to this cause would not be so quickly apparent from an examination of the excretions as would one due to a flushing out of the tissues. For this reason the increase in the excretion of P_2O_5, although relatively as great as that of nitrogen, did not appear until the second day of the copious water drinking.

It might be well to add that there was nothing in any of our experiments which would lead one to infer that there was anything detrimental in the consumption of large volumes of water. On the contrary, there are many good reasons for advocating copious water drinking. As is of course well known, the functions of an organism are satisfactorily fulfilled only when the tissues are well supplied with water. An impairment of the normal functions of digestion, assimilation, and elimination must speedily follow a subnormal decrease in the water supply of the daily dietary. At the same time copious water drinking increases peristalsis, biliary secretion, and arterial tension, and reduces the body temperature.

XIV. CONCLUSIONS.

Copious water drinking causes an increased excretion of nitrogen and phosphorus by the urine. The increase in the amount of nitrogen eliminated is due, *primarily*, to the washing out of the tissues of the urea previously formed, but which has not been removed in the normal processes, and, *secondarily*, to a stimulation of proteid catabolism.

The increase in the excretion of phosphorus is due to increased cellular activity and the accompanying catabolism of nucleins, lecithins, and other phosphorus-containing bodies.

In man an increase of 4500 c.c. in the daily amount of water ingested, after the organism had been brought to nitrogen equilibrium by means of a constant diet fed during a preliminary period of three days, caused an increase of 1.415 grams or 12.8 per cent., in the excretion of nitrogen

by the urine on the first day, and the somewhat smaller increase of 0.755 gram or 6.8 per cent., upon the second day. Therefore the total influence upon the excretion of nitrogen by the urine produced by the ingestion of 9000 c.c. of water additional in a period of forty-eight hours was to cause an increase of 2.47 grams during that period. This was an average daily increase of 1.085 grams or 9.8 per cent., above the normal output.

In other experiments additions of 3100 c.c. of water to the constant diet caused increases in the excretion of nitrogen by the urine, varying from 0.83 gram or 5.9 per cent., to 1.12 grams or 9.5 per cent., for the first day, and from 0.38 gram or 2.7 per cent., to 0.78 gram or 6.6 per cent., for the second day.

The course of the SO_3 excretion, while somewhat irregular, still showed a general tendency to run parallel with that of nitrogen. A daily addition of 4500 c.c. of water for a period of two days caused an increase of 0.265 gram or 15.6 per cent., in the SO_3 excretion by the urine on the first day, and one of 0.195 gram or 11.6 per cent., on the second day. When the amount of water added daily during a period of forty-eight hours was 3100 c.c. the increase upon the first day varied from 0.205 gram or 10 per cent., to 0.085 gram or 4.1 per cent. On the second day there was an increase of 0.128 gram or 6.2 per cent. In one experiment the SO_3 excretion was decreased on the days in which 3100 c.c. of water was added to the diet, the decreases varying from 0.309 gram or 20.9 per cent., to 0.016 gram or 0.81 per cent., for the first day, and from 0.258 gram or 14.1 per cent., to 0.124 gram or 6.3 per cent., for the second day.

The course of the P_2O_5 excretion, as influenced by copious water drinking, was distinctly different from that of nitrogen or SO_3. In every instance the excretion of P_2O_5 was increased above the normal on each day of the water period, the maximum excretion occurring, with absolute regularity, on the second day of the increased water ingestion. A daily addition of 1500 c.c. of water, for a period of forty-eight hours, caused an increase of 0.22 gram or 9.1 per cent., upon the first day, and one of 0.4 gram or 17.1 per cent., upon the second day. An addition of 3100 c.c. of water under similar conditions caused increases in the excretion of P_2O_5 by the urine varying from 0.011 gram or 0.43 per cent., to 0.238 gram or 10.6 per cent., for the first day, and from 0.096 gram or 3.7 per cent., to 0.459 gram, or 20.5 per cent., for the second day.

There was a constant tendency for the largest percentage of the ingested fluid to be excreted by the urine on the days of copious water drinking. This was indicated by an elimination of 28.5 per cent. on an ingestion of 2300 c.c. of fluid, as compared with an elimination of 90.6 per cent. on an ingestion of 6400 c.c. of fluid.

The thanks of the author are due Professor John Marshall for many suggestions during the preparation of this article.

TABLE A.—DIET: AMOUNT AND COMPOSITION.

Experiment I.

Food.	Water. Per ct.	Fat. Per ct.	Ash. Per ct.	N. Per ct.	SO_3. Per ct.	P_2O_5. Per ct.	Amount of food eaten per day. Grams.
Milk (fresh)	.....	4.16	.....	0.42	0.13	0.25	1800
Butter	8.81	.....	2.51	.....	.....	.....	75
Crackers	8.38	5.87	1.77	1.60	0.25	0.22	330

TABLE B.—EXCRETION OF N, SO_3 AND P_2O_5.

Experiment I.

Number of experimental day.	Subject.	Body weight (Kilograms).	Urine. Vol.	Sp.gr.	Reaction.	N. Per cent.	N. Grms.	SO_3. Per cent.	SO_3. Grms.	P_2O_5. Per cent.	P_2O_5. Grms.	Nature of the diet.
I.	I	61.51	1090	1.018	Acid.	1.11	12.10	.....	.....	.....	.....	Normal.
II.	"	61.47	997	1.020	"	1.11	11.10	0.165	1.65	0.241	2.41	"
III.	"	61.43	770	1.023	"	1.43	11.03	0.223	1.72	0.294	2.27	"
IV.	"	61.39	5250	1.005	"	0.24	12.48	0.037	1.95	0.049	2.56	1500 c.c. water added daily.
V.	"	61.29	5800	1.005	"	0.20	11.82	0.032	1.88	0.047	2.74	
VI.	"	61.47	1275	1.016	"	0.86	10.91	0.113	1.83	0.195	2.49	Normal.
VII.	"	61.64	1160	1.018	"	10.1	11.73	0.160	1.85	0.200	2.31	"
VIII.	"	61.57	1110	1.020	"	0.98	11.17	0.154	1.76	0.192	2.19	"
IX	"	61.25	885	1.024	"	1.21	11.01	0.190	1.68	0.254	2.25	"

TABLE C.—INCOME AND OUTGO OF NITROGEN.

Experiment I.

Subject.	Experimental period.	Length of period. Days.	Nitrogen (grams). In food.	In urine.	In feces.	Gain or loss (+ or —).	Average gain or loss per day.	Nature of the diet.
I	I.	2	25.68	22.13	2.95	+ 0.60	+ 0.30	Normal.
"	II.	2	25.68	24.30	3.067	— 1.687	— 0.844	4500 c.c water added daily.
"	III.	4	51.36	41.82	4.568	+ 1.972	+ 0.493	Normal.
	Total	8	102.72	91.25	10.585	+ 0.885	+ 0.110	

TABLE D.—INCOME AND OUTGO OF SO_3.

Experiment I.

Subject	Experimental period	Length of period. Days.	SO_3 (grams). In food.	In urine.	In feces.	Gain or loss (+ or —).	Average gain or loss per day.	Nature of the diet
I	I	2	6.33	8.37	3.01	— 0.08	— 0.01	Normal.
"	II.	2	6.33	3.83	3.09	— 0.59	— 0.30	4500 c.c. water added daily.
"	III	4	12.66	7.12	5.06	+ 0.48	+ 0.12	Normal.
	Total	8	25.32	14.32	11.19	— 0.19	— 0.09	

TABLE E.—INCOME AND OUTGO OF P_2O_5.

Experiment I.

Subject.	Experimental period.	Length of period Days.	P_2O_5 (grams). In food.	In urine.	In feces.	Gain or loss (+ or —).	Average gain or loss per day.	Nature of the diet.
I.	I.	2	10.452	4.68	4.78	+ 0.992	+ 0.496	Normal.
"	II.	2	10.452	5.30	4.72	+ 0.432	+ 0.216	4500 c.c. water added daily.
"	III.	4	20.904	9.24	9.31	+ 2.354	+ 0.588	Normal.
	Total	8	41.808	19.22	18.81	+ 3.778	+ 0.472	

TABLE F.—ANALYSIS OF FECES.

Experiments I., II., and III.

Experiment.	Subject	Period.	Length of period. Days.	Amount of feces (grams).	N. Per cent.	N. Grms.	SO_3. Per cent.	SO_3. Grms.	P_2O_5. Per cent.	P_2O_5. Grms.
I.	I.	I.	3	103.0	4.30	4.429	4.43	4.57	6.96	7.17
"	"	II.	2	72.0	4.26	3.067	4.29	3.09	6 55	4.72
"	"	III.	4	108.0	4.23	4.568	4.68	5.06	8.62	9.31
II.	II.	I.	3	46.5	3.34	1.554				
"	"	II.	2	45.2	3.45	1.56				
"	"	III.	1	22.8	3.45	0.79				
"	III.	I.	3	53.0	3.53	1.872				
"	"	II.	2	38.6	3.48	1.34				
"	"	III.	1	19.2	3.48	0.67				
III.	IV.	I.	2	40.9	3.95	1.62	4.25	1.74	9.24	3.78
"	"	II.	2	48.8	4.11	2.01	3.90	1.90	8.99	4.39
"	V.	I.	2	36.0	4.31	1.55	5.33	1.92	10.63	3.83
"	"	II.	2	35.7	3.77	1.35	5.40	1.93	11.31	4.04
"	"	III.	2	38.2	3.76	1.44	4.73	1 81	10.10	3.86

TABLE G.—DIET: AMOUNT AND COMPOSITION.

Experiment II.

Food.	Water. Per ct.	Ash. Per ct.	Fat. Per ct.	Nitrogen. Per ct.	Nitrogen. Grams. Per meal	Nitrogen. Grams. Per dy.	Amount of food taken per day. Grams.
Milk: Composite* (partially dry).	5.30	5.270	4.42†	3.81			
Fresh . . .	.....	.....	.....	0.54	2.970	8.910	1650
Butter	8.77	.....	.....	0.195	0.039	0.117	60
Crackers . . .	7.82	1.848	5.94	1.755	1.755	5.265	300
Totals . .	.....	.....	.....	.....	4.764	14.292	

* Composite milk = 14.22 per ct. P. D.
† Ether extract.

TABLE H.—EXCRETION OF N, SO_3 and P_2O_5.

Experiment II.

No. of experimental day.	Subject.	Urine. Grams.	Sp.gr.	Reaction.	N. Per cent.	N. Grms.	SO_3. Per cent.	SO_3. Grms.	P_2O_5. Per cent	P_2O_5. Grms.	Nature of the diet.
I.	II.	975 0	.....	.....	1.34	13.02	0.205	1.997	0.257	2.509	Normal.
II.	"	1111.0	.. ..	.....	1.24	13.79	0.176	1.957	0.248	2.756	"
III.	"	972.0	.....	.....	1.22	11.84	0.203	1.976	0.248	2.406	"
IV.	"	3796.0	1.005	Acid.	0.38	14.45	0.051	1.950	0.068	2.568	3100 c.c. water added.
V.	"	4757 1	1.001	"	0.26	12.43	0.039	1.842	0.056	2.653	3100 c.c. water added.
VI.	"	1568.0	1.014	"	0.66	10.32	0.114	1 787	0.117	1.840	Normal.
I.	III.	711.5	.....	.....	1.66	11.82	0.279	1.986	0.298	2.120	"
II.	"	656.5	.....	.....	1.78	11.66	0.272	1.786	0.347	2.275	"
III.	"	737.0	.....	.....	1.62	11.96	0.243	1.793	0.316	2.330	"
IV.	"	2549.8	1.008	Acid.	0.51	12.93	0.058	1.480	0.097	2.479	3100 c.c. water added.
V.	"	4844.2	1.005	"	0.26	12.59	0.032	1.531	0.056	2.700	3100 c.c. water added.
VI.	"	1691.2	1.014	"	0.70	11.89	0.105	1.775	0.128	2.167	Normal.

TABLE I.—INCOME AND OUTGO OF NITROGEN.

Experiment II.

Subject.	Experimental period.	Length of period (days).	Nitrogen (grams). In food.	In urine	In feces.	Gain or loss (+ or —).	Average gain or loss per day.	Nature of the diet.
II.	I.	3	42.87	38.762	1.554	+ 2.554	+ 0.851	Normal.
"	II.	2	28.58	26.88	1.560	+ 0.180	+ 0 09	3100 c.c. water added daily.
"	III.	1	14.29	10.32	0.790	+ 3.180	+ 3.180	Normal.
	Total	6	85.74	75.962	3.904	+ 5.874	+ 0.979	
III.	I.	3	42 87	35.44	1.872	+ 5.558	+ 1.852	Normal.
"	II.	2	28.58	25.52	1.340	+ 1.720	+ 0.860	3100 c.c. water added daily.
"	III.	1	14.29	11.89	0.670	+ 1.730	+ 1.730	Normal.
	Total	6	85.74	72.85	3.882	+ 9.008	+ 1.501	

TABLE J.—DIET: AMOUNT AND COMPOSITION.

Experiment III.

Food.	Water. Per ct.	Fat. Per ct.	Ash. Per ct.	N. Per ct.	SO_3. Per ct.	P_2O_5. Per ct.	Amount of food eaten per day. Grams.
Milk* (composite partially dried)	3.48	34.09 Ether extract 4.2	4.38	4.41	1.21	2.02	
Milk (fresh) . .	.....		.....	0.56	0.15	0.26	1650
Butter	8.56	.....	2.67	.....	.....	.....	60
Crackers . . .	9.47	6.20	1.92	1.84	0.28	0.24	300

* Milk (partially dried) = 12.71 per cent.

Table K.—Excretion of N, SO_3 and P_2O_5. Experiment III.

Number of experimental day	Subject	Urine: Grams	Sp. gr.	N: Per cent.	N: Grms.	SO_3: Per cent.	SO_3: Grms.	P_2O_5: Per cent.	P_2O_5: Grms.	Nature of the diet
I.	IV.	1,185.7	....	1.170	14.26	0.176	2.145	0.248	3.027	Normal.
II.	"	1655.3	....	0.830	13.80	0.120	1.997	0.170	2.823	"
III.	"	4557.9	1.007	0.326	14.86	0.047	2.156	0.067	3.061	3100 c.c. water added.
IV.	"	4460.7	1.007	0.323	14.41	0.046	2.038	0.076	3.393	3100 c.c. water added.
I.	V.	768.6	....	1.72	13.26	0.266	2.047	0.354	2.724	Normal.
II.	"	680.6	....	1.98	13.48	0.298	2.032	0.412	2.808	"
III.	"	3545.8	1.009	0.407	14.43	0.063	2.214	0.081	2.883	3100 c.c. water added.
IV.	"	3980.0	1.008	0.35	13.95	0.054	2.167	0.075	3.002	3100 c.c. water added.
V.	"	1220.0	1.020	1.12	13.70	0.171	2.093	0.232	2.834	Normal.
VI.	"	861.4	1.024	1.54	13.32	0.210	2.075	0.326	2.812	"

Table L.—Income and Outgo of Nitrogen. Experiment III.

Subject	Experimental period	Length of period (days)	Nitrogen (grams): In food	In urine	In feces	Gain or loss (+ or −)	Average gain or loss per day	Nature of the diet
IV.	I	2	29.72	28.06	1.62	+ 0.04	+ 0.02	Normal.
"	II	2	29.72	29.27	2.01	− 1.56	− 0.78	3100 c.c. water added daily.
	Total	4	59.44	57.33	3.63	− 1.52	− 0.38	
V.	I	2	29.72	26.71	1.55	− 1.43	+ 0.71	Normal.
"	II	2	29.72	28.38	1.35	− 0.01	− 0.005	3100 c.c. water added daily.
	III	2	29.72	27.02	1.44	+ 1.26	+ 0.63	Normal.
	Total	6	89.16	82.11	4.34	− 2.68	0.45	

Table M.—Income and Outgo of SO_3. Experiment III.

Subject	Experimental period	Length of period (days)	SO_3 (grams): In food	In urine	In feces	Gain or loss (+ or −)	Average gain or loss per day	Nature of the diet
IV.	I	2	6.71	4.142	1.74	− 0.858	+ 0.429	Normal.
"	II	2	6.71	4.191	1.99	− 0.646	+ 0.323	3100 c.c. water added daily.
	Total	4	13.48	8.333	3.73	− 1.504	+ 0.376	
V.	I	2	6.74	4.079	1.92	+ 0.741	+ 0.37	Normal.
"	II	2	6.74	4.411	1.98	+ 0.399	+ 0.20	3100 c.c. water added daily.
"	III.	2	6.74	4.168	1.81	+ 0.762	+ 0.381	Normal.
	Total	6	20.22	12.658	5.66	+ 1.902	+ 0.317	

Table N.—Income and Outgo of P_2O_5. Experiment III.

Subject.	Experimental period	Length of period (days).	P_2O_5 grams: In food.	In urine.	In feces.	Gain or loss (+ or −).	Average gain or loss per day.	Nature of the diet.
IV.	I	2	9.92	5.850	3.78	+ 0.29	+ 0.145	Normal.
"	II	2	9.92	6.451	4.39	− 0.921	− 0.462	3100 c.c. water added daily.
	Total	4	19.84	12.304	8.17	− 0.631	− 0.158	
V.	I.	2	9.92	5.532	3.83	+ 0.558	+ 0.279	Normal.
"	II.	2	9.92	5.885	4.01	− 0.005	− 0.0025	3100 c.c. water added daily.
"	III.	2	9.92	5.646	3.86	+ 0.414	+ 0.207	Normal.
	Total	6	29.76	17.063	11.73	+ 0.967	+ 0.161	

Table O.—Percentage of Ingested Water Excreted by the Urine.

Experiment.	Number of experimental day.	Subject.	Volume of fluid ingested, c.c.	Volume of urine, c.c.	Volume of ingested fluid in excess of vol. of urine.	Percentage of ingested fluid recovered
I.	I.	I.	1,900	1090	810	57.4
"	II.	"	1,900	997	903	52.5
"	III.	"	1,900	770	1130	40.5
"	IV.	"	6,400	5250	1150	82.0
"	V.	"	6,400	5800	600	90.6
"	VI.	"	1,900	1275	625	67.1
"	VII.	"	1,900	1160	740	61.0
"	VIII.	"	1,900	1140	760	60.0
"	IX.	"	1,900	885	1015	46.6
	Total	.....	26,100	18367	7733	70.4
II.*	I.	II.	2,300	975.0	1325.0	42.4
"	II.	"	2,300	1111.0	1189.0	48.3
"	III.	"	2,300	972.0	1328.0	42.3
"	IV.	"	5,400	3796.0	1604.0	70.3
"	V.	"	5,400	4757.1	642.9	88.1
"	VI.	"	2,300	1568.0	732.0	68.0
	Total	.....	20,000	13179.1	6820.9	65.8
"	I.	III.	2,300	711.5	1588.5	30.9
"	II.	"	2,300	656.5	1643.5	28.5
"	III.	"	2,300	737.0	1563.0	32.0
"	IV.	"	5,400	2549.8	2850.2	47.2
"	V.	"	5,400	4844.2	555.8	89.7
"	VI.	"	2,300	1691.2	608.8	73.5
	Total	.....	20,000	11190.2	8809.8	55.9
III.*	I	IV.	2,300	1218.7	1081.3	52.9
"	II.	"	2,300	1655.3	644.7	71.9
"	III	"	5,400	4557.9	842.1	84.4
"	IV.	"	5,400	4460.7	939.3	82.6
	Total	.....	15,400	11892.6	3507.4	77.2
"	I.	V.	2,300	768.6	1531.4	33.4
"	II.	"	2,300	680.6	1619.4	29.6
"	III.	"	5,400	3545.8	1854.2	65.6
"	IV.	"	5,400	3980.0	1420.0	73.7
"	V.	"	2,300	1220.0	1080.0	53.0
"	VI.	"	2,300	861.4	1438.6	37.4
	Total	.....	20,000	11056.4	8943.6	55.2

* The figures for the daily output of urine for Experiments II. and III. are grams instead of cubic centimetres.

Bibliography.

1. Voit. Untersuchungen über den Einfluss des Kochsalzes, des Kaffees und der muskelbewegungen auf den Stoffwechsel, München, 1860, p. 61.
2. Panum. Nordiskt. medicinskt. Arkiv, 1874; Jahresbericht für Thierchemie, 1874, 4.
3. E. Salkowski. Quoted by Dubelir, Zeitschrift für Biologie, 28.
4. Feder. Zeitschrift für Biologie, 17; and Zeitschrift fur Biologie, 14.
5. Falck. Beiträge zur Physiologie, Hygiene, Pharmacologie und Toxicologie, i., Stutgart, 1875.
6. Munk. Virchow's Archiv, 1883, xciv. p. 449; and 1880, lxxx. p. 43.
7. Stohmann, Rost und Frühling. Quoted by Dubelir, Zeitschrift für Biologie, 28.
8. Weiske, Kennepohl und Schulze. Zeitschrift für Biologie, 17.
9. Bartels. Greifswalder med. Beiträge, iii. 6.
10. Smith. British Medical Journal, 1861.
11. Meyer. Zeitschrift für klinische Medicin, 1880, ii. p. 34.
12. Winternitz. Wiener medizinische Jahrbücher, 1864, ii. p. 20.
12a. Edsall. Publications from the William Pepper Laboratory of Clinical Medicine, 1900, vol. i.
13. Mosler. Archiv des Vereins fur wissenschaftliche Heilkunde, ii. p. 398.
14. Weiske. Journal für Landwirtschaft, 1874; Jahresbericht fur Thierchemie, 1874, 4.
15. Kaupp. Vierordt's Archiv, 1856.
16. Rosemann. Archiv für die gesammte Physiologie, 1898, lxxii. p. 467.
17. Böcher. Quoted by Schöndorff, Archiv fur die gesammte Physiologie, 46.
18. Bidder und Schmidt. Die Verdauungssäfte und der Stoffwechsel, 1852.
19. Ter-Grigorianz. Inaugural Dissertation, St. Petersburg, 1886, p. 40; Bulletin 45, Office of Experiment Stations, United States Department of Agriculture.
20. Rubner. Zeitschrift für Biologie, xvii. p. 221.
21. Forster. Quoted by Feder, Zeitschrift für Biologie, 1878, xiv. p. 175.
22. Becher. Zeitschrift für rationelle Medicin, 1855, 6.
23. Schöndorff. Archiv fur die gesammte Physiologie, xlvi. p. 529; Jahresbericht für Thierchemie, 1890, 20.
24. Salkowski. Quoted by Feder, Zeitschrift fur Biologie, xvii p. 562
25. Eichorst. Archiv für die gesammte Physiologie, iv. p. 570.
26. Weigelin. Archiv fur Anat., Physiol. und Wissensch. Medicin, Leipzig, 1868.
27. Genth. Untersuchungen uber den Einfluss des Wassertrinkens auf den Stoffwechsel, Wiesbaden, 1856.
28. Bischoff. Der Harnstoff als Maass des Stoffwechsels, 1853.
29. Foster. Text-book of Physiology, p. 631.
30. Henneberg. Futterung der Wiederkauer, 1860; Bulletin 45, Office of Experiment Stations, United States Department of Agriculture.
31. Oppenheim. Archiv fur die gesammte Physiologie, xxiii. p. 165. Jahresbericht fur Thierchemie, 1880, 10.
32. Neumann. Archiv fur Hygiene, 1899, pp. 35–36; Experiment Station Record, Department of Foods and Animal Production, 1900, xi., No. 8.
33. Matzkevich. Inaugural Dissertation, St. Petersburg, 1890; Bulletin 45, Office of Experiment Station, United States Department of Agriculture.
34. Gruzdiev. Vrach (St. Petersburg), xi. p. 213; Bulletin 45, Office of Experiment Stations, United States Department of Agriculture.
35. Dubelir. Zeitschrift für Biologie, xxviii. p. 237.
36. Seegen. Wiener Akademie Sitzungsberichte, 1871, 63; Jahresbericht für Thierchemie, 1871, i.
37. Frankel. Archiv für Pathologie, Anatomie und Physiologie, 1876, 67.
38. Karchagin. Vrach (St. Petersburg), x. p. 453; Bulletin 45, Office of Experiment Stations, United States Department of Agriculture.
39. Roux. Archive de physiologie normale et pathologique, 1874, tome i.
40. Speck. Wiener medizinische Jahrbücher, 1864, i. p. 198.
41. Gley et Richet. Comptes-rendus de la Société de biologie, Paris, 1887, viii. 4.
42. J. W. Paton. Journal of Anatomy and Physiology, 1871, 5.
43. Landauer. Ungarisch. Archiv fur Medicin, 1895, 3.
44. Straub. Zeitschrift für Biologie, 1899, xxxviii. 4.
45. Von Noorden. Pathologie des Stoffwechsels, Berlin, 1893.

THE PROCEEDINGS OF THE SOCIETY OF NORMAL AND PATHOLOGICAL PHYSIOLOGY, UNIVERSITY OF PENNSYLVANIA.

Meeting of December 19, 1904.

The Effect of Removal of Oxygen from a Nerve Trunk upon its Power of Conducting Impulses.

Dr. Edward Lodholz.

Von Beyer studied (*Zeit. für Allgemein. Phys.*, vol. i.) the effect of removing oxygen from the nerve trunk of a frog by means of chemical agents. He reports that when reduced iron moistened with oxygen-free normal saline solution was applied to a nerve, response to electric stimulation soon disappeared, but returned when the iron was washed away. These experiments were repeated, with the object of studying the effect of reduced iron upon the conductivity of nerves. A nerve-muscle preparation of the frog was arranged in a Sherrington moist chamber in the usual manner. Two platinum electrodes were brought in contact with the nerve, one near the spinal column, the other close to the muscle. Between these electrodes reduced iron was applied. Central and peripheral stimulation was made every twenty minutes. When temporaria were used, in an hour or two central stimulation produced no effect; whereas, the peripheral end of the nerve was still irritable. The removal of the iron was often followed by a return of a normal response when the central end was stimulated. These experiments seemed to demonstrate that conductivity is lessened in a nerve by extracting oxygen. However, the same results could often be obtained when no reduced iron was applied. The investigation suggested the possibility that von Beyer obtained his results because he experimented with temporaria, an animal which shows inconstant reac-

tions, particularly in summer. For this reason the esculenta were substituted. It was found when the nerve of this animal was exposed for six hours to the action of iron no lessening in conductivity was manifest.

A Study of the Conditions Following the Establishment of the Eck Fistula in Dogs.

Dr. P. B. Hawk.

A series of feeding and injection experiments upon dogs in which the liver function was greatly impaired by the successful performance of Eck's operation. The operations were in each instance performed by Dr. J. E. Sweet. Six dogs were experimented upon, the experimental periods being from twenty-eight to one hundred and thirty-five days in length. A short summary of a typical feeding experiment follows: Dog No. 2. Fed mixed diet eleven days, and on the following four days beef-meal (predigested powdered beef) and milk. On the afternoon of the fourth day of this diet there was pronounced ataxia, entire loss of sight and hearing, complete anæsthesia, and catalepsy. In about four hours the symptoms began to abate, and on the next day had entirely disappeared. The animal fasted for twenty-four hours, and was then placed on a diet of *fresh* lean beef. On the morning of the fifth day of this diet symptoms were observed similar to those occurring after the beef-meal diet. Placed on a diet of milk and bread, the animal died on the fifty-ninth day of the experiment. A poor appetite and a loss of 42 per cent. body weight were noted. Autopsy showed the fistula opening to be about 2 cm. long. There was no collateral circulation.

In other experiments the typical symptoms enumerated above occurred only after the feeding of lean beef and Liebig's extract daily for at least one week.

Contrary to the finding of Pawlow, the feeding of sodium carbamate and the injection of this salt into the blood stream of normal dogs were productive of none of the symptoms noted above. Injections of Liebig's extract under these conditions were also negative.

Meeting of January 16, 1905.

Do the Salts of the Germicidal Acids Possess Germicidal Properties?

Dr. Horatio C. Wood, Jr.

It is well known that salicylic acid, benzoic acid, and other members of this group are actively germicidal, but their slight solubility interfere with their use as practical disinfectants. The sodium salts of these acids are freely soluble, and if they possessed the bactericidal properties of the acid they would be of great value. Experiments were made to elucidate this problem upon bacteria obtained by exposing nutrient bouillon to the air until it was thoroughly cloudy, and then adding to this bouillon varying strengths of salicylic or benzoic acid and inoculating from this at different intervals into sterile bouillon.

It was found that one minute's contact with 0.5 per cent. salicylic acid solution destroyed the organisms, but that after ten minutes' exposure to a 2 per cent. solution of sodium salicylate a good growth was obtained.

Similarly with benzoic acid a 0.6 per cent. solution of the acid prevented growth after five minutes' contact, but a good growth occurred after five minutes' exposure to a 2 per cent. solution of sodium benzoate. It was found that bacteria would not develop in bouillon containing 1 per cent. of sodium salicylate.

It would seem, therefore, that the sodium salts of these acids are slightly antiseptic, but far inferior in germicidal power to the acids themselves.

A Schematic Eye: An Instrument for the Luminous Demonstration of the Functions of the Various Parts of the Eye, of Normal and Abnormal Refraction, and of the Application of Glasses Throughout the Whole Range of Disorders of Refraction.

Prof. Edward T. Reichert.

The apparatus has been designed especially for the use of students. The lenses are of the standard test-case size. Among the numerous important phenomena that may satisfactorily be demonstrated are: the effects of different kinds and strengths of lenses; the optical axis; the first and second principal foci; the "far" and "near" points; the effects of lenses not properly centred; the functions of the iris; the mechanism of accommodation; Scheiner's experiment; the inversion of the image; variations in the size of the retinal image; spherical aberration; chromatic aberration; irradiation; vision after the removal of the lens or cornea; vision in gray cataract; hyperopia and its correction; myopia and its correction; presbyopia and its correction; self-adaptation to abnormalities in refraction; the correction for squint; corneal astigmatisms in all forms, and their correction; various entoptic phenomena, such as lens shadows, Purkinje-Sanson figures, opacities of the cornea, effects of displacement of the lens or eyeball; binocular vision, identical points, correction for the blind spot, etc.

With a test-case set every error of refraction that can be corrected by the ophthalmologist by such a set can be produced and corrected in such a manner that all of the phenomena can be clearly seen.

Meeting of January 30, 1905.

The Experimental Production of Monsters.

Prof. Edwin G. Conklin.

In the unsegmented eggs of the Ascidian, *Cynthia partita*, all of the germinal layers and most of the important organs of the larva, or tadpole, are represented by distinct kinds of protoplasm, which occupy definite regions of the egg. The first cleavage lies in the median plane and divides all of these substances bilaterally; the second cleavage is at right angles to this and separates the anterior from the posterior half. In the anterior half is contained all of the substance of the nervous system and notochord; in the posterior half, all of the substance which forms the muscular system.

When any of the cleavage cells are killed the remaining ones develop just as if the egg were still entire. One of the first two cells gives rise to a right or left half-embryo; the two anterior cells produce the anterior half of an embryo, with notochord and neural plate, but without any trace of muscles; the two posterior cells produce the posterior half of an embryo, with muscles, but without a trace of notochord or nervous system.

Studies on Cell Granula.

Prof. Leo Loeb.

This communication will appear in full in the Bulletin.

BOOK REVIEWS.

A Treatise on Bright's Disease and Diabetes: With Especial Reference to Pathology and Therapeutics. By James Tyson, M.D. Including a Section on the Ocular Changes in Bright's Disease and Diabetes, by George E. de Schweinitz, M.D. Second edition, illustrated. Philadelphia: P. Blakiston's Son & Co.

Twenty years after its original publication Tyson's *Bright's Disease and Diabetes* has just appeared in its second edition. It has been to a considerable extent rewritten and enlarged, several colored plates having been added to the text, as have also a number of histological drawings. The ophthalmological chapters, the work in the original edition of the late Professor Wm. F. Norris, have in the present edition been written by his successor to the chair of Ophthalmology, Professor George E. de Schweinitz, and are illustrated by colored plates of ocular fundi.

The work is written in a scholarly and painstaking manner, considerable space being devoted to historical considerations, and debatable points being interestingly discussed in a manner commensurate with the author's authority on subjects to which he has given life-long attention.

Of course there have been oversights. Thus, no mention is made of the recent work done on the role of the thyroid gland in neutralizing systemic intoxication due to renal insufficiency; nor is lumbar puncture mentioned in connection with the treatment of uræmia. While making frequent allusions to the increased blood pressure which is noted in chronic interstitial nephritis, no consideration is given to the sphygmanometer either in the practical or theoretical discussion of the subject. While the value of such functional tests of renal insufficiency as the elimination of sodium chloride, methylene blue, etc., are still *sub judice*, they might have received consideration. The value of the book would also be enhanced if the index were made more extensive.

The latter part of the book deals under systematized headings with Diabetes Mellitus and Insipidus, the chapters devoted to these subjects being as exact as the present state of our knowledge of these still obscure diseases will permit.

On the whole, the volume can be thoroughly and unhesitatingly recommended as a valuable book of reference on the subjects of which it treats. G. W. N.

Obstetrics for Nurses. By Joseph B. de Lee, M.D., Professor of Obstetrics, Northwestern University Medical School; Obstetrician to Mercy, Wesley, Provident, Cook County, and Chicago Lying-in Hospitals; Lecturer in the Nurses' Training School of same. Fully illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

When Dr. de Lee wrote this book he intended it primarily for nurses, but as it contains so much of real value along all the branches of midwifery it must be considered a good book as well for the medical student and practitioner, they often being forced to perform the duties of a nurse in the conduct of their obstetric cases; and the former especially will find this book useful, as his early years of practice will probably be spent among individuals not able to employ nurses, or, if a nurse, such a one as will need instruction in every duty assigned her. The subject is considered from two viewpoints: obstetrics for nurses and the actual obstetric nursing. The two subjects are skilfully combined, so that their relations are natural and helpful. The author has taught this branch of medicine for eight years to nurses of four different training schools. The illustrations, which are plentiful, are nearly all original, and were made expressly for this book; the photographs were made from actual scenes. Excellent features of the book are chapters on hospital *vs.* home nursing, a dietary for nurses, and a glossary; the latter contains most of the terms employed in this branch of medicine. E. L.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. I of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

THE EFFECT OF TUBERCULOSIS VACCINATION UPON CATTLE INFECTED WITH TUBERCULOSIS.[1]

By Leonard Pearson, B.S., V.M.D.,
State Veterinarian of Pennsylvania,

and

S. H. Gilliland, V.M.D., M.D.,
Bacteriologist of the State Livestock Sanitary Board of Pennsylvania.

During recent years a large amount of work has been done by Koch, Trudeau, de Schweinitz, von Behring, Maragliano, Fraenkel, and others, for the purpose of discovering and developing a specific treatment for tuberculosis. This work has taken various directions, and has included experiments wherein the toxins of tubercle bacilli have been administered and experiments wherein antitoxins found in the blood of animals that have been treated with toxins have been used. Toxins of various kinds have been employed; from the original and new tuberculin of Koch to the toxalbumin, the watery tuberculin, the tubercle bacilli deprived of fat of Maragliano, and bacillary pulp.

The antitoxins that have been used have been developed as a result of the injection of the various toxins mentioned above, and also living tubercle bacilli of low virulence.

The reports of the therapeutic experiments made upon infected animals with tuberculosis toxins and antitoxins are numerous, but cannot be regarded as convincing. Most of these experiments have been made upon rabbits and guinea-pigs. Neither rabbits nor guinea-pigs are altogether satisfactory for experiments of this kind; the former because of their comparative immunity to tubercle bacilli of the human type, the latter on account of their excessive vulnerability to inoculation tuberculosis of either of the mammalian types. Enough work has been done to denote that the progress of a tuberculous infection may be controlled in some degree by specific means. It is important that these various methods shall be compared and measured both quantitatively and qualitatively. There is here a large and important field of labor for the critical experimentalist.

Among the means that have been proposed for controlling the spread of tuberculosis among cattle is vaccination, or the inoculation of animals with living cultures of tubercle bacilli of low virulence for the animals upon which they are inoculated. This method of producing artificial immunity has been the subject of considerable study both in this country and in Europe, and has been reported upon to this society by the writers of this paper.

[1] Read before the Pathological Society of Philadelphia Dec. 22, 1904.

In connection with some tuberculosis vaccination experiments made by the writers, the opportunity occurred to test the effect of vaccination upon some young cattle already infected with tuberculosis. As this treatment appears to have had a decided effect upon the course of the disease in the infected animals treated, it is considered that our observations should be placed upon record, especially since the work covered nearly two years, long enough to show definite results, and is the first of the sort of which we have knowledge.

In testing with tuberculin a large herd of shorthorn and grade shorthorn cattle in December, 1902, that was known to have been infected with tuberculosis for a number of years, it was found that practically all of the members of the herd responded affirmatively to the test. Among the animals so responding were twelve calves from six to eight months old. As these calves had mingled rather freely with the members of the herd, and as they had been reared on the milk of extensively tuberculous cows, it was not surprising to find that they responded to the tuberculin test. These twelve calves were obtained for use in this experiment. They were shipped to Philadelphia and were placed in a temporary building on the grounds of the veterinary school, where they were kept apart from other cattle.

The twelve calves were again tested with tuberculin February 2, 3, 1903. All responded to this test. They were then weighed and divided into two lots, of six each, as nearly equal as possible in respect to age, size, weight, and condition. One of these lots was subdivided into two groups of three each.

The three calves of one of the sub-groups were given seven intravenous injections of a standard suspension[1] in water of tubercle bacilli of human type (culture M). The dosage began at 1 c.c. and was increased to 6 c.c. The

[1] By a standard suspension is here meant a suspension of tubercle bacilli in water in such quantity as to give an opacity equal to that of a twenty-four-hour culture of typhoid bacilli in bouillon; 1 c.c. of such a suspension is estimated to contain the equivalent of 0.0013 gram of tubercle bacilli dried ten days in a desiccating chamber over calcium chloride.

intervals between injections were from six to twenty days, and the period covered was from February 9 to May 1, 1903, as is shown by the protocols. These same calves received another and final intravenous injection of 5 c.c. of a standard suspension of living tubercle bacilli (culture M) about a year later, March 29, 1904.

The three calves of the second sub-group were given subcutaneous injections of tuberculin at intervals of from two to ten days. The injections of tuberculin were repeated until the hypersensitiveness of the animal to tuberculin had disappeared, after which the calves received an intravenous injection of a suspension of tubercle bacilli (culture M) in water. Following each intravenous injection of living tubercle bacilli, the animal was again given tuberculin a number of times until its hypersensitiveness to tuberculin again disappeared. The procedure in these cases in respect to the order of the injections of tuberculin bacilli was as follows: Two subcutaneous injections of tuberculin, an intravenous injection of tubercle bacilli, six injections of tuberculin, an injection of tubercle bacilli, six injections of tuberculin, an injection of tubercle bacilli, three injections of tuberculin. The period of treatment extended from February 9 to April 30, 1903, inclusive; the exact times of administration and the doses are shown by the protocols. The calves of this group, as of the first group described, were given an intravenous injection of 5 c.c. of standard suspension of living tubercle bacilli (culture M) March 29, 1904. Following this, tuberculin was administered five times at intervals of three or four days.

The remaining six calves were given no treatment whatever, but were, at all times, kept with the six calves under treatment; so that all of the twelve calves in this experiment were subjected to the same conditions of life and subsisted upon the same kind and quantity of food.

All of the calves were kept in a stable until May 29, 1903, when they were placed upon pasture, which became very scanty during the latter part of the season. During the winter of 1903–04 the cattle were fed mixed hay, corn fodder, and a grain mixture of bran and corn meal. Only a little grain was fed. About the middle of May, 1904, the cattle (now about two years old) were again placed on pasture, where they remained until they were killed at the close of the experiment.

Two cattle, both controls, died; the first one May 5, 1903; the second September 13, 1904; two, one control and one treated, were killed April 4, 1904, and the rest were killed in September, 1904.

When the cattle in this experiment died or were killed they were submitted to careful post-mortem examination. Material was stained for examination for tubercle bacilli and guinea-pigs were inoculated from the lesions of some of them. Histological examinations of the lesions were made by Dr. C. Y. White, to whom we are greatly indebted for reports upon his examinations.

The treatments and post-mortems are summarized in the following protocols:

First Group. *Three calves that received intravenous injections of tubercle bacilli alone.*

Fig. 1.—*Red Bull* (16,013).

1902.	December	19.	0.1 c.c. tuberculin; reaction.				
1903.	February	2.	0.8 c.c.	"	"	to 106.2° F.	
"	"	9.	0.0013 grm. human tubercle bacilli, intravenously.				
"	"	18.	0.0032	"	"	"	"
"	March	2.	0.0039	"	"	"	"
"	"	21.	0.0039	"	"	"	"
"	April	4.	0.0052	"	"	"	"
"	"	10.	0.0065	"	"	"	"
"	May	1.	0.0078	"	"	"	"
1904.	March	29.	0.0065	"	"	"	"
"	September	15.	Killed.				

Fig. 1.

Right lung. Left bronchial gland.

Necropsy. Weight 643 pounds; fair condition. The lesions of tuberculosis found in this animal were as follows: At the lower border of the middle lobe of the right lung was a slightly depressed area about one-half inch in diameter containing a collection of thick yellow pus filling a cavity the size of a large pea. The walls of this cavity are one-eighth of an inch thick, white, and of firm, dense texture. In one of the left peribronchial glands there is a caseocalcareous nodule about the size of a pea and having the appearance of a wholly closed process. Guinea-pigs inoculated from the lesion in the lung became tuberculous.

Fig. 2.—*Red-and-white Bull* (16,017).

1902.	December	19.	0.1 c.c. tuberculin; reaction.				
1903.	February	2.	0.8 c.c.	"	"	to 105.6° F.	
"	"	9.	0.0013 grm. human tubercle bacilli, intravenously.				
"	"	18.	0.00325	"	"	"	"
"	March	2.	0.0026	"	"	"	"
"	"	21.	0.0039	"	"	"	"
"	April	4.	0.0052	"	"	"	"
"	"	10.	0.0065	"	"	"	"
"	May	1.	0.0078	"	"	"	"
1904.	March	29.	0.0065	"	"	"	"
"	September	15.	Killed.				

Fig. 2.

Postpharyngeal gland.
Left bronchial gland.
Mediastinal gland, middle and posterior.

Necropsy. Weight 467 pounds; good condition. The following lesions of tuberculosis were found: In one of the left peribronchial glands a yellow, caseous area one-tenth of an inch in diameter. In the posterior mediastinal gland there is an area the size of a pea, yellow in color and quite calcareous, surrounded by a white, dense capsule. In the middle mediastinal gland there is a similar area, though much smaller, being but one-twelfth of an inch in diameter. In one of the postpharyngeal glands there is a caseocalcareous area one-half of an inch in diameter, surrounded by an unusually thick, dense, white, fibrous wall. The caseous collection contains many calcareous grains. There are also in this gland three other similar areas, much smaller, about one-eighth of an inch in diameter, and each is surrounded by a dense capsule. In addition to this evidence of tuberculosis it was observed that both lungs, although generally well inflated, were heavy, soggy, somewhat leathery and without elasticity. There were some small areas where the tissues were contracted and dense. Histologically these areas show numerous dense bands of connective tissue. The bloodvessels are very much thickened. In limited areas some of the smaller ones are almost obliterated. Some of the smaller sublobules show the lung tissue to be collapsed or organized. The peribronchial lymphatic tissue is increased and the pleura is thickened. There is no caseation or evidence of a tubercular process excepting as above noted. Guinea-pigs inoculated with the caseocalcareous material from the thoroughly encapsulated lesions in the postpharyngeal glands became tuberculous.

Fig. 3.—*Rosa Heifer* (16,021).

1902	December	19	0.1 c.c. tuberculin; reaction	
1903	February	2	0.8 c.c.	" to 106° F.
"	"	9	0.0013 grm. human tubercle bacilli, intravenously	
"	"	18	0.0026	" "
"	March	2	0.0026	" "
"	"	21	0.0039	" "
"	April	1	0.0052	" "
"	"	10	0.0052	" "
"	May	1	0.0065	"
1904	March	29	0.0065	
"	September	15	Killed	

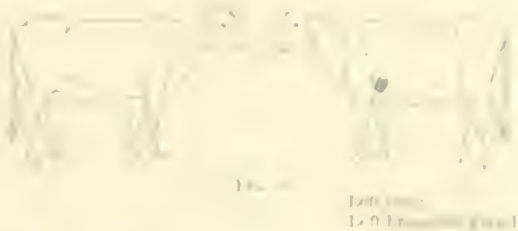

Fig. —
[illegible]
1-5 [illegible] gland

Necropsy. Weight 465 pounds; good condition. The evidence of tuberculosis here consists in a very dense condition of the lower half of the posterior flap of the anterior lobe of the left lung, which is attached to the posterior lobe and to the pericardium and the diaphragm. This dense mass consists of a very thick wall of fibrous tissue surrounding a sequestrum of lung tissue, about one and a half inches in its anteroposterior and two and a half inches in its vertical diameter. Above this mass the lung tissue of the anterior lobe contains an excessive quantity of fibrous tissue appearing as white bands between the lobules. These bands are quite firm and are from one-eighth to one-quarter of an inch wide. The parenchyma surrounded by these bands is studded with fine dots and lines of white, consisting of fibrous tissue. Above this sclerotic zone the lung tissue is elastic and pink. There are nowhere nodules or caseous areas, excepting in one of the left peribronchial glands which contains a caseocalcareous nodule the size of a pea.

There is reason to believe that in this animal there has been an extensive area of tuberculous tissue in the lower portion of the anterior lobe of the left lung. This area appears to have become encysted and the lung tissue above to have been the seat of numerous small tubercles which were transformed into scar tissue and appear now very much hardened and contracted.

Second Group. *Three calves which received intravenous injections of tubercle bacilli alternating with repeated subcutaneous injections of tuberculin.*

Fig. 4.—*Red-and-white Heifer* (16,015).

1902.	December	19.	0.1 c.c. tuberculin; reaction.	
1903.	February	2.	0.8 c.c.	" " to 105.8° F.
"	"	9.	1.0 c.c.	" " to 102.8° F.
"	"	15.	1.5 c.c.	" " to 103.0° F.
"	"	18.	0.0026 grm. human tubercle bacilli, intravenously	
"	"	22.	1.0 c.c. tuberculin; reaction	to 103.0° F.
"	"	24.	1.5 c.c.	" " to 102.6° F.
"	March	4.	2.0 c.c.	" " to 104.6° F.
"	"	6.	2.5 c.c.	" " to 102.8° F.
"	"	11.	3.0 c.c.	" " to 103.0° F.
"	"	14.	3.5 c.c.	" " to 103.0° F.
"	"	21.	0.0039 grm. human tubercle bacilli, intravenously.	
"	"	27.	1.0 c.c. tuberculin; reaction	to 103.2° F.
"	"	29.	1.5 c.c.	" " to 103.0° F.
"	April	5.	2.0 c.c.	" " to 102.6° F.
"	"	8.	2.5 c.c.	" " to 102.2° F.
"	"	10.	3.0 c.c.	" " to 101.0° F.
"	"	16.	3.5 c.c.	" " to 103.6° F.
"	"	18.	0.0052 grm. human tubercle bacilli, intravenously	
"	"	23.	0.5 c.c. tuberculin; reaction	to 104.6° F.
"	"	27.	1.0 c.c.	" " to 102.6° F.
"	"	30.	2.0 c.c.	" " to 103.6° F.
1904	March	29.	0.0065 grm. human tubercle bacilli, intravenously.	
"	April	1.	1.0 c.c. tuberculin; reaction	to 102.8° F.
"	"	3.	2.0 c.c.	" " to 103.3° F.
"	"	8.	3.0 c.c.	" " to 102.4° F.
"	"	11.	3.0 c.c.	" " to 102.9° F.
"	"	15.	5.0 c.c.	" " to 103.8° F.
"	September	15.	Killed.	

Fig. 4
1-5 bronchial gland

Necropsy. Weight 566 pounds; good condition. The only evidence of tuberculosis in this animal is a calcareous nodule one-eighth of an inch in diameter situated in one of the left peribronchial glands. This nodule is sharply differentiated from the surrounding adjacent, quite normal glandular tissue, and has the appearance of a completely closed process. Guinea-pigs inoculated with an emulsion of this nodule developed tuberculosis.

FIG. 5.—*Red-and-white Heifer* (16,019).

1902.	December	19.	0.1 c.c. tuberculin ; reaction.		
1903.	February	2.	0.8 c.c.	"	" to 105.6° F.
"	"	9.	1.0 c.c.	"	" to 103.4° F.
"	"	15.	1.5 c.c.	"	" to 102.8° F.
"	"	18.	0.0026 grm. human tubercle bacilli, intravenously.		
"	"	22.	1.0 c.c. tuberculin ; reaction to 104.0° F.		
"	"	24.	1.5 c.c.	"	" to 103.8° F.
"	March	4.	2.0 c.c.	"	" to 103.8° F.
"	"	6.	2.0 c.c.	"	" to 103.2° F.
"	"	11.	3.0 c.c.	"	" to 104.2° F.
"	"	14.	3.5 c.c.	"	" to 103.8° F.
"	"	21.	0.0039 grm. human tubercle bacilli, intravenously.		
"	"	27.	1.0 c.c. tuberculin ; reaction to 104.6° F.		
"	"	29.	1.5 c.c.	"	" to 102.6° F.
"	April	5.	2.0 c.c.	"	" to 102.8° F.
"	"	8.	2.5 c.c.	"	" to 103.2° F.
"	"	10.	3.0 c.c.	"	" to 102.6° F.
"	"	16.	3.5 c.c.	"	" to 103.0° F.
"	"	18.	0.0052 grm. human tubercle bacilli, intravenously.		
"	"	23.	0.5 c.c. tuberculin ; reaction to 102.8° F.		
"	"	27.	1.0 c.c.	"	" to 102.4° F.
"	"	30.	2.0 c.c.	"	" to 103.8° F.
1904.	March	29.	0.0065 grm. human tubercle bacilli, intravenously.		
"	April	1.	1.0 c.c. tuberculin ; reaction to 102.9° F.		
"	"	4.	2.0 c.c.	"	" to 103.0° F.
"	"	8.	3.0 c.c.	"	" to 103.0° F.
"	"	11.	4.0 c.c.	"	" to 103.8° F.
"	"	15.	5.0 c.c.	"	" to 102.4° F.
"	September	15.	Killed.		

FIG. 5.
Left bronchial gland.

Necropsy. Weight 580 pounds; good condition. One of the left peribronchial glands contained two nodules, each about one-tenth of an inch in diameter. Both are distinctly calcareous and are sharply differentiated from the immediately adjacent, quite normal gland tissue.

The right lung is rather dense and leathery and contains some collapsed areas. In such a collapsed area there is found an infiltration of round cells surrounding the bronchial walls. The lymphatic nodes in the same region are greatly increased. The alveoli are œdematous and in some places the exudate has undergone organization.

There is no evidence of caseation or of tuberculosis in the lungs or elsewhere, excepting as noted in the left peribronchial gland.

FIG. 6.—*Red Heifer* (16,022).

1902.	December	19.	0.1 c.c. tuberculin ; reaction.		
1903.	February	2.	0.8 c.c.	"	" to 105.2° F.
"	"	9.	1.0 c.c.	"	" to 103.0° F.
"	"	15.	1.5 c.c.	"	" to 101.4° F.
"	"	18.	0.0013 grm. human tubercle bacilli, intravenously.		
"	"	22.	1.0 c.c. tuberculin ; reaction to 103.2° F.		
"	"	24.	1.5 c.c.	"	" to 104.0° F.
"	March	4.	2.0 c.c.	"	" to 105.6° F.
"	"	6.	2.5 c.c.	"	" to 103.8° F.
"	"	11.	3.0 c.c.	"	" to 103.2° F.
"	"	14.	3.5 c.c.	"	" to 104.0° F.
"	"	21.	0.0039 grm. human tubercle bacilli, intravenously.		
"	"	27.	1.0 c.c. tuberculin ; reaction to 103.4° F.		
"	"	29.	1.5 c.c.	"	" to 102.8° F.
"	April	5.	2.0 c.c.	"	" to 102.6° F.
"	"	8.	2.5 c.c.	"	" to 102.8° F.
"	"	10.	3.0 c.c.	"	" to 103.2° F.
"	"	16.	3.5 c.c.	"	" to 103.4° F.
"	"	18.	0.0039 grm. human tubercle bacilli, intravenously.		
"	"	23.	0.5 c.c. tuberculin ; reaction to 103.6° F.		
"	"	27.	1.0 c.c.	"	" to 102.2° F.
"	"	30.	2.0 c.c.	"	" to 104.2° F.
1901.	March	29.	0.0065 grm. human tubercle bacilli, intravenously.		
"	April	1.	1.0 c.c. tuberculin ; reaction to 103.0° F.		
"	"	4.	2.0 c.c.	"	" to 103.3° F.
"	"	8.	3.0 c.c.	"	" to 103.8° F.
"	"	11.	4.0 c.c.	"	" to 103.1° F.
"	"	15.	5.0 c.c.	"	" to 102.2° F.
"	"	30.	Killed.		

FIG. 6.
Left bronchial gland.

Necropsy. Weight 421 pounds; unthrifty condition. The only distinct evidence of tuberculosis in this animal is a calcareous nodule the size of a pea in the left bronchial gland. The pleura and peritoneum were more or less opaque and showed films or flakes of fibrin partly or wholly organized and in some places evidently of considerable age. Guinea-pigs inoculated from the calcareous nodule in the bronchial gland became tuberculous.

It is evident that this animal had suffered with a widespread inflammation of the serous membranes from which it had practically recovered. Such a diffuse inflammation of the serous membranes of both visceral cavities occurs in tuberculosis of cattle of the type of pearl disease. But in this case there were no tubercles or evidence of tuberculosis. One must consider the possibility that in this animal there was a healed, fresh tuberculosis of the pleura and peritoneum.

THIRD GROUP. *Six calves which received no treatment and were kept as controls for the purpose of comparison.*

FIG. 7.—*Red-and-white Bull* (16,014).

1902.	December	19.	0.1 c.c. tuberculin ; reaction.		
1903.	February	2.	0.8 c.c.	"	" to 105.6° F.
"	May	4.	Died.		

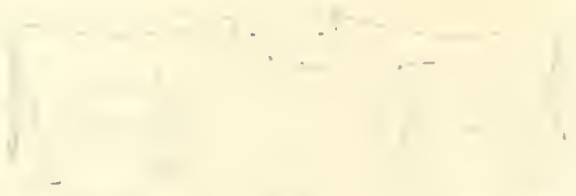

Fig. 7.

Right bronchial gland. Left bronchial gland.
Mediastinal glands.

Necropsy. Weight 430 pounds. This bull died suddenly, apparently of acute indigestion. The only evidence of tuberculosis in this animal consisted in the presence of several caseous nodules in both bronchial and in the mediastinal lymphatic glands.

Fig. 8.—*Red-and-white Heifer* (16,016.

1902. December 19. 0.1 c.c. tuberculin ; reaction.
1903. February 2. 0.8 c.c. " " to 106.0° F.
1904. September 17. Killed.

Fig. 8.

Left lung.
Mediastinal gland.

Necropsy. Weight 578 pounds; poor condition. In the left lung at the bottom of the posterior lobe there is an area containing numerous tubercles, some of which have undergone caseation. Two similar areas are found in the tip of the lung. The surrounding lung tissue is red and dense and is infiltrated with small gray tubercles of pinhead size, some of which have cheesy centres. The posterior mediastinal gland is five inches long and two inches in diameter. This gland is filled with dense nodules, most of which have undergone caseation, and some of which contain calcareous deposits. Guinea-pigs inoculated with infiltrated lung tissue developed tuberculosis.

Fig. 9.—*Red-and-white Heifer* (16,018.)

1902. December 19. 0.1 c.c. tuberculin ; reaction.
1903. February 2. 0.8 c.c. " " to 106.4° F.
1904. September 19. Killed.

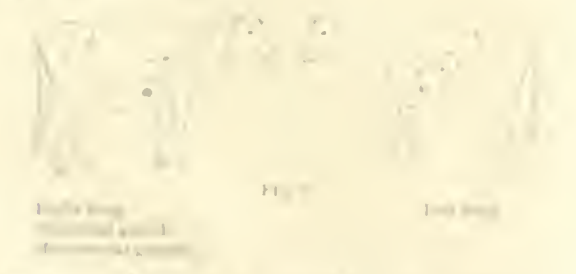

Fig. 9.

Left lung.

Necropsy. Weight 415 pounds; poor condition. Both the anterior and middle lobes of the right lung are attached to the chest wall, the anterior lobe is also attached to the pericardium. There are numerous tuberculous areas of all ages and up to one and a half inches in diameter scattered rather thickly through both lungs. Both bronchial and the mediastinal glands are enlarged and contain numerous caseous and caseocalcareous nodules.

Fig. 10.—*Red-and-white Bull* (16,020).

1902. December 19. 0.1 c.c. tuberculin ; reaction.
1903. February 2. 0.8 c.c. " " to 105° F.
1904. September 13. Died.

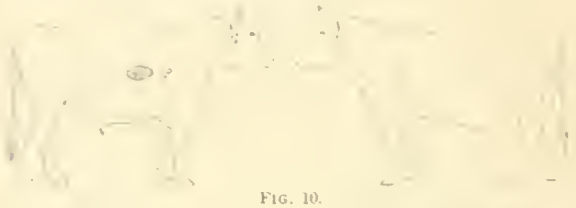

Fig. 10.

Bronchial glands. Postpharyngeal glands.
Mediastinal glands. Bronchial glands.
Postpharyngeal glands.

Necropsy. Weight 480 pounds; fair condition. This bull was apparently quite healthy on the 12th of September, and was found dead in the stable the next day. It was found that there was a great collection of gas in the paunch and this appears to have been the cause of death, through interference with respiration by pressure upon the diaphragm. The evidence of tuberculosis in this animal consisted in the presence of several caseous nodules in both bronchial glands; the posterior mediastinal gland is six inches long and quite thick. The entire structure of this gland has undergone degeneration. Both postpharyngeal lymphatic glands are slightly enlarged and contain caseous areas.

It is quite possible that in this case the enlarged mediastinal lymphatic gland was a contributing cause of death through pressing upon the œsophagus and tending to interfere with the regurgitation of gas.

Fig. 11.—*Red-and-white Heifer* (16,023).

1902. December 19. 0.1 c.c. tuberculin ; reaction.
1903. February 2. 0.8 c.c. " " to 106.1° F.
1904. April 30. Killed.

Fig. 11.

Left lung etc.

Necropsy. Weight 313 pounds; very poor condition, this heifer was killed because it was in such bad condition that it could not live long.

The costal pleurae of both sides are coated with masses

of round and flattened nodules occurring singly and in patches. The largest patch is nearly a foot in diameter and about two inches thick. Both lungs are covered with round and flattened nodules, some of which are closely attached to the pleura and some of which hang from the pleura singly and in clusters. There is a fringe around the borders of the lungs about two inches wide and very thickly studded with hard nodules, the centres of which have undergone caseation. Both lungs contain a large number of caseous areas. The bronchial and mediastinal lymphatic glands are considerably enlarged and caseous. The postpharyngeal glands are in similar condition. The omentum, the walls of the stomachs, the abdominal walls, the spleen and liver are coated with nodular masses that are characteristic of pearl disease. There are numerous caseous areas in the substance of the liver. The bronchial lymphatic glands are enlarged to several times their natural size and are caseous.

This is a case of "pearl disease" in the most advanced form and of widest distribution.

FIG. 12.—*Red-and-white Bull* (16,024).

1902. December 19. 0.1 c.c. tuberculin ; reaction.
1903. February 2. 0.8 c.c. " " to 106° F.
1904. September 17. Killed.

FIG. 12.

Right lung.
Right bronchial gland.

Necropsy. Weight 524 pounds; good condition. The right bronchial gland is somewhat enlarged and contains a calcareous nodule. In the anterior lobe of the right lung there are numerous nodules containing pus. These are surrounded by firm, fibrous walls. The intervening lung tissue is collapsed.

The observations here recorded show a decided difference between the lot of six young cattle that were treated and the six that were not treated. Since the two lots of animals were in all respects as nearly equal as possible at the beginning of the experiment, and since they were cared for all together and in precisely the same way, excepting in respect to specific treatment, it is but fair to conclude that the six treated animals were favorably influenced by the treatment.

We believe that we have sufficient evidence to justify the statement that the treatment to which six of the animals were subjected had the effect not only of keeping in check the progress of the tuberculous process, but in causing a distinct and in some cases (Nos. 2, 3, and 6) a great retrogression of the lesions. In other words, the treatment had a distinct curative effect.

In all of the treated animals the lesions were quiescent and encapsulated. But they contained living tubercle bacilli. There is room for difference of opinion as to whether an animal or a person in which there is a tuberculous lesion containing living bacilli may be regarded as cured. If the lesion is wholly cut off by a thick fibrous wall from living tissue and if it is incapable of again becoming active, it would appear that a claim for a cure might fairly be entered. But how is one to know that activity may not be re-established? If there is resistance enough to cause the complete encapsulation of all tuberculous lesions in the body, it is evidence that a considerable degree of immunity had been developed. If the bacilli in the lesions are of such low virulence that they cannot infect an animal of the species of the one in which they are found, renewed activity is not to be expected. De Schweinitz found living tubercle bacilli in minute nodules in the lungs of a cow inoculated intravenously a year before with bacilli of human type that appear to have been incapable of producing progressive disease. Nodules may occur from intravenous injections of dead tubercle bacilli. Fraenkel and von Behring have found in lesions of tuberculosis of cattle tubercle bacilli that are not pathogenic for cattle.

Unfortunately, in these experiments, the virulence for cattle of the tubercle bacilli in the lesions in the treated animals was not determined.

These experiments which were made on a few young cattle in the earlier stage of tuberculosis do not justify conclusions or inferences as to the probable effect of similar treatment on older and more extensively diseased animals. Experiments must be made on a larger and broader scale. We have at this time a number of animals under treatment which we hope will give us more knowledge on this subject.

But we hold that the experiments that have been made show clearly that under such treatment as was given tuberculous lesions do not extend; on the contrary, that they recede and that new implantations do not occur even upon prolonged contact with tuberculous herd mates.

A STUDY OF THE PATHOLOGICAL CHANGES IN SOME MOUND-BUILDERS' BONES FROM THE OHIO VALLEY, WITH ESPECIAL REFERENCE TO SYPHILIS.

By Samuel Torrey Orton, B.S.

Not infrequently among the skeletal remains of the Mississippi and Ohio Valley mound-builders are found bones exhibiting very evident gross pathological changes. The Museum of the Ohio State Archæological and Historical Society at the Ohio State University in Columbus has among its rich collection quite an amount of this material, and through the kindness of Mr. Wm. C. Mills, the curator of the museum, some of the bones were obtained for examination, the results of which are given below.

During the summers of 1899 and 1900 the Society's exploration party were at work on what is known as the Baum Village site, and a short account of this work is appended here as descriptive of the general source of the material. The village site lies on the Baum farm in the valley of Paint Creek, one of the smaller tributaries of the Scioto River, whose valleys make up much of Ohio's richest farm land. The village had been apparently roughly semicircular in outline, standing at that time, in all probability, on a point of land jutting out into Paint Creek (now about one-half mile distant), and having as its centre a mound about sixteen feet high and forty feet in diameter. This mound was explored about ten years ago by a party from the Smithsonian Institute, and a report of the findings there show by comparison with material from the village site that the two were beyond doubt isochronological. This statement also holds true with reference to the other mounds, village sites, and mound-builders' remains of the Ohio and Mississippi valleys.

The site is now a part of a cultivated field, and the surface of the ground is scattered for a space of an acre or more with bits of shell and bone, and fragments of pottery turned up by the plow. This ground, however, had all been worked over before the advent of the steel plow-share, and on going down from the surface an average depth of three feet the earth contains flakes of flint, arrow-heads, bones of various wild animals, ashes, charcoal, broken fresh water mussel-shells, and other refuse of the village, with a sharp line of demarcation between the "worked" loam above and the gravel "hard-pan" below. Scattered here and there throughout this area were found places where the soft loam continued down below the general depth, and on removal of the earth here these proved to be pits from three to six feet in diameter and of an equivalent depth filled with much the same material as was scattered through the surface soil, but in greater abundance. These refuse pits proved a fertile field for exploration, and in them, though not exclusively, were found in addition to the things mentioned above numerous implements and ornaments, such as shell and bone beads, bone awls and fish-hooks, hide scrapers carved from the metatarsal bones of the deer, shell and bone amulets and pendants, flint arrow and spear points, charred cobs of the maize, charred bits of cloth and shells of nuts (including the hazel, hickory, butternut, and black walnut), ashes in great heaps, broken pottery, split and shattered bones of all of our common small wild animals, and also of the mountain lion, bear, elk, and deer, and an occasional human skeleton. The majority of the human burials had been made, however, in the surface soil, most of them on the sandy gravel substratum, although some had so shallow a covering as to have been disturbed by the plows. All of the bones were in an exceedingly good state of preservation considering their undoubted age, and this is accounted for probably in part by the topography and constitution of the soil in which they were buried, which favored quick and full drainage of surface water, and in part by the great quantities of wood ashes with which they were more or less surrounded. One or two of the bodies had been buried in rough stone coffins built of large, flat, unshapen slabs of the slaty limestone of the neighborhood, but for the most part no attempt was made to enclose the bodies, which were interred apparently in the very back yard of their premises. The remains were buried in the recumbent position, with no regular arrangement in regard to the points of the compass, as is sometimes seen, and were more or less scattered throughout the whole area.*

As will be seen below the lesions of the bones examined are such as to lead to the diagnosis of syphilis as their etiological factor. The reader of works on the history of syphilis will find interest in the discussions of many syphilographers and historians on the origin of this now almost universal disease. The French writers especially have taken up the argument, and we find opinion divided between three possibilities: (1) That the disease was endemic both in this continent and the old world before communication was established across the Atlantic. (2) That the origin of the infection was in the American races, and that it was carried to Europe by the sailors of Columbus' expedition on their return; and, (3) the reverse of the latter theory—*i. e.*, that its place of endemicity was in Europe, and that it was brought westward to this side of the Atlantic by Columbus' men and so implanted here.

It will be readily seen that the results of the present investigation have no bearing on the two former hypotheses.

* At one place, however, some skeletons were uncovered in one small area; these bones were on exhibition in their relative positions in the enclosure at the centre of the Anthropological Building at the Pan-American Exposition in Buffalo in 1901.

If the diagnosis given is correct, in view of the undoubted pre-Columbian time of these remains, it is entirely incompatible with the third explanation. It may well be added here, however, that the supporters of this theory are comparatively few.

A vast amount of literature has been published in discussion of this question, and strong arguments brought to bear on all sides.

The work of Buret[1] in support of the universal pre-Columbian distribution brings up some very strong proofs. These volumes, while of only a semiscientific nature, give a *résumé* of a great amount of evidence of various worth. Early in the first volume is an account of lesions found on human osseous remains exhumed at Solutrè in the Department of Saône-et-Loire in western France. These bones, found buried with those of the horse and reindeer and cut flints, etc., belonging to the Gallo-Roman or Merovingian epochs, were referred by anthropologists of the best authority to the Stone Age, and, the author adds, "examined by Broca, Ollier, Parrot, and Virchow, the lesions were, by common consent, pronounced syphilitic." Then follow reports of examinations of several Peruvian prehistoric skulls showing evidences of acquired and hereditary syphilis and, by way of contrast, lesions which from their description seem identical, on bony remains from the caverns and dolmens inhabited by "tribes who peopled the Gauls during the Stone Age and in the druidical times before the Frankish dynasties." In another chapter is given an abstract of translations from Chinese documents collected by the Emperor Hoang-ty, 2637 B.C., and forming the volume Hoang-ty-mi-King or the *Medical Treatise of Hoang-ty.* Quotations of this translation give very apt descriptions of the two main varieties of venereal ulcers with reference to the connection between the Hunterian sore and the secondary eruption, with an account of the varieties of the latter which is easily recognizable, and as treatment advise mercurial frictions, aided by an oily mixture and a powder composed of mercury.* In support of the existence of syphilis in Biblical times, during the ascendancy of the Greeks and Romans and in the Middle Ages, is quoted a mass of documents largely secular which show beyond doubt that venereal diseases of some kind were rampant then, and would seem to indicate the probability of the existence of lues venerea, but hardly prove the point.

On the other side the discussion was headed by Astruc,[2] the early French syphilographer. His articles, while able, were written before the discovery of many important pieces of evidence, and hence are not of such worth as the work of Bloch,[3] which is among the most recent writing on the subject.

Bloch credits the appearance of the disease in Europe to the return of Columbus' first expedition and its rapid dissemination to the debauchery of the troops of Henry the VIII. of France on his expedition against Naples and their widespread dispersion, carrying the infection with them, at the end of the siege. He uses the malignancy of the epidemic of Naples as an argument in support of his theory that European peoples were before that outbreak free from the disease and consequently lacked that immunity which would obtain through long exposure of the race to infection. To quote directly: "Wenn der Syphilis schon Jahrtausende bestanden hätte, dann hätte doch im Laufe dieser langen Zeit ein so grosse Immuniseirung der Völker des Orbis antiquus gegen das syphilitische Gift eintreten müssen dass die ereignisse am ende des 15 Jahrhunderts einfach unmöglich gewesen wären."

He asks how else can the early appearance of the secondary lesions, the high fever, the pain, the high mortality, etc., in the Neapolitan outbreak be explained. It seems not untenable to believe that the infection had been present on both sides of the Atlantic for thousands of years and that in this way the virus may have become attenuated in each continent—so much so in Europe as to have been overlooked during the dark era of the Middle Ages, or to have been confounded with leprosy or other current diseases—and to have owed its virulence in the epidemic of 1495–6 to a transplantation of the infection of American origin on to what might be for it a favorable soil. Evidences of this variability in infective agencies is seen sometimes in cases where inhabitants of a notorious typhoid centre remain free from infection for indefinite periods only to succumb to the disease on removal to another endemic focus. Here also may be mentioned the severity of the venereal infections brought back by our own troops from the Philippines. One author has spoken of the organism of gonorrhœal infection from this source as the micrococcus gonorrhœæ malignus.

Considerable work has been done on the lesions found in the bones of the prehistoric or at least pre-Columbian inhabitants of this country with the result of a diagnosis of syphilis. Among this are the investigations of Jones[4] in 1876 and 1878, of Brühl[5] in 1880 and 1890, and of Hyde[6] in 1891, all of which are articles of interest and of great value to a study of this question.

If the evidence quoted above from Buret of the early existence of syphilis in China be granted, its presence on the American continent in pre-Columbian times might be considered as an addition to the theory, upheld by some anthropologists of repute, that the prehistoric inhabitants of this hemisphere found their way here from northeastern China and Siberia, across Behring Straits to Alaska, and thence down the Pacific coast to be widely scattered from there over the whole continent.

* It is of interest here to mention also the account of vaccination against variola practised by the Hindoo physicians 1000 years B.C., by taking the liquid of the pustule of the cow's teat or from the arm of a human being, placing it upon the point of a lancet and introducing it into the arm of the patient to be vaccinated, mixing the fluid with the blood, etc.

With regard to the pathology of the specimens under examination a considerable handicap is apparent in that the cellular constituents of the bones are long since disintegrated, but the lesions of the resistant parts are sufficiently characteristic to permit of diagnosis. These changes in the hard parts in syphilitic diseases exclusive of the cellular study are reviewed here for comparison with the results to be shown presently.

All authors agree on the subject that the bones most frequently the seat of syphilitic changes are those which are most exposed to trauma, which seems to act as a focalizing factor for the morbid process. The order of preference given is: the tibia, clavicle, cranium, ulna, sternum, ribs, etc. This is notoriously the distribution of lesions found in the mound-builders. One particular skeleton is recalled in which gross changes were apparent in both tibiæ, the vault of the cranium, one clavicle, and one ulna, and this was noted before the sites of election of the syphilitic processes were known to the observer, and, indeed, before syphilis was suspected as being a factor in the case. The following figures furnished by Mr. Mills will show something of the distribution: Of 127 skeletons exhumed at the Baum Village site 21 were diseased. Fully 60 per cent. of those affected show the lesions worst upon the tibia, the ulna coming next perhaps, then the cranium and then the sternum. But few ribs were affected.

Given the disease attacking a long bone Lang[7] says: "It is interesting to note that the diaphyses are much more frequently affected than their epiphyses."

Again, all authors seem in accord with the statement that the two processes of osteoporosis and osteosclerosis occurring side by side in adjacent portions of the same bone are almost pathognomonic of syphilis. Hyde and Montgomery[8] put it thus: "These processes of rarefaction, bone formation, and even bone degeneration to the point of production of a sequestrum through an ulcerative opening may occur simultaneously in different parts of one bone or side by side, one lamella thickening while that adjacent softens. This multiformity of processes is a characteristic feature of bone syphilis . . . . In examination of bones with a view to determine the probable causes of death the existence of worm-eaten cavities, of irregular thickenings, and of perforations of entire plates of bone is indicative of syphilis."

Le Baron[9] describes a syphilitic tibia in these terms: "Near the middle of the crest of the tibia there exist a considerable hyperostosis of the anterior half of the diaphysis. As a result the anterior border presents a very marked curve with an anterior convexity. This hypertrophy has an elongated, ovoid form, and its surface is as smooth as the rest of the bone. It extends to a length of 85 mm. In this locality the tibia is 24 mm. thick. A longitudinal section made through the tumor shows that it is composed of compact tissue. The medullary canal has preserved its normal dimensions."

In this quotation the word "hyperostosis" is used apparently to describe an overgrowth of a portion of the bone, but not of its entirety, which latter seems to be the accepted meaning. Thus the *American Text-book of Genitourinary Diseases, Syphilis, and Diseases of the Skin*[10] defines hyperostosis as an enlargement of the *whole* bone, exostosis as a large growth on the bone, and osteophytes as small, superficial elevations.

The gross changes brought about by the syphilitic process in long bones consist of one or more large exostoses (rarely a hyperostosis) in the diaphysis. In the tibia, for instance, the exostosis is usually single when well advanced and is a large, ovoid hypertrophy, most frequently in the upper half of the shaft, although sometimes the whole of the diaphysis is involved. This new growth of bone to be typical shows both in the gross section and microscopically the condition of rarefying osteitis side by side with one of condensing osteitis which may be far enough advanced to justify the term "eburnation." In any given specimen, however, the lesions may be chiefly confined to any one of these three types, dependent on the progress of the disease—but the other types are always present to a greater or less degree. There may be also on the surface of the bone small osteophytes either of intense hardness when they are, as a rule, more or less regular and polished, or when they occur in the line of origin or insertion of a muscle roughened, irregular projections.

Sometimes the exostosis, which is nearly always on the anterior aspect of the bone (that part exposed to trauma), may involve the entire length of the diaphysis, giving a curve of large radius with convexity forward and distorting the whole of the bone except the epiphyses, which seem to be entirely normal. This gives rise to the condition called "sabre-blade" deformity when occurring in the tibia, where it is most frequently seen. The lumen of the medullary canal may be enlarged through absorption of the bone surrounding it. This may be greater or less than, or equal to, the deposition of bone from the periosteal side, thus giving a large canal with thin walls or thick walls with an increased lumen, or an increased lumen with walls of about normal thickness. Sometimes deposition of bone takes place from the endosteum, encroaching on the medullary canal either through the formation of dense bone or through a mesh of very fine interlacing spicules of osseous material, almost or entirely filling up the original canal. The external surface of an exostosis of a long bone may be as smooth as, or even smoother than, the normal bone surface, in which case the condition of sclerosis will usually be found to be the predominant one, or it may be marked with irregular lines or depressions more or less parallel with the long diameter of the shaft, or deeply grooved with branching channels in which lay the enlarged periosteal vessels, or filled with small holes running into the body, which on section prove to be enlarged Haversian canals perpendicular

to the shaft. The perpendicular arrangement of the new canals is explained by Cornil and Ranvier[11] as follows: "The direction of the Haversian canals follows that of the bloodvessels. The periosteal or granulation vessels come from the Haversian canals at the surface of the bone and it is around these vessels that the new osseous lamellæ are formed."

In the skull the process is essentially the same—*i. e.*, rarefaction in some areas with sclerosis in others. The sclerosis here often takes the form of small, exceedingly dense, smooth, eburnated bosses or osteophytes or in an increase of bony substance in the cancellous diploë, sometimes progressing to such an extent as to obliterate the vascular spaces there, to which process some authors ascribe the necrosis which is associated with the syphilitic lesions in the cranium and is so noticeably absent elsewhere. In the words of Cornil and Ranvier: " . . . il est bien certain que la mort de l'os resulte souvent d'une osteite condensante ou sclerosé, poussee jusqua l'obliteration des canaux vasculaires."

Differential diagnosis is here made from tuberculosis, chronic osteomyelitis, and osteitis deformans. The pathological changes of bone syphilis are so clear and well defined, however, as not to require elaborate differentiation. Osteitis deformans while a rare disease, now, is included in view of the fact that so little is known of the diseases prevalent at the time from which our material has come. In the osseous lesions of tuberculosis and chronic osteomyelitis the formation of an involucrum with sequestra and cloacæ is usually a prominent feature. In the tuberculous bone affections the disease is very often manifested in the epiphyses and joints and leaves there unmistakable traces of its ravages. Lazarus-Barlow[12] is quoted here: "Tuberculous disease of bones differs in the fact that sclerosis is almost characterized by its absence. . . . It is never found that a focus of tuberculous disease shows a considerable formation of new bone in the neighborhood of the principal seat of the disease. The utmost that we see is the presence of a few osteophytic growths." Again, the same author says of osteitis deformans: "All bones are usually affected and the whole bone is involved." This is a true hyperostosis of general distribution rather than exostosis on certain selected bones as is the case in syphilis.

The microscopic picture of bone syphilis exclusive of the cellular changes is directly comparable to the gross lesions—*i. e.*, concurrent rarefying and condensing osteitis. Cornil and Ranvier, in describing the result of rarefaction by enlargement of the Haversian canals, says: " . . . The canals communicate and by their junction form irregular spaces filled with marrow of an embryonal type." Simes and White in their translation of Cornil's *Syphilis*[13] describe the sclerotic changes as follows: "When under the influence of appropriate treatment or following the natural course of the malady, the inflammation ceases and the disease retrogrades, there is seen a reparation of the diseased and partially destroyed bone. . . . There result new lamellæ with new osteoblasts, and these form several series parallel one with another, or follow the irregular arrangement of the Haversian canals. This exuberant formation of new osseous lamellæ may constitute beneath the periosteum exostoses of varying size and in the bone a parenchymatous exostosis or eburnation." Again in Shakespeare and Simes' translation of Cornil and Ranvier's work appears the following: "A transformation which has taken place in consequence of the formation of osseous tissue which being deposited in the interior of the canals has narrowed them. The new osseous layers may be so arranged that the lumen of the canal does not correspond to the centre of the original canal. This process continuing the canal may be completely obliterated so that at the centre of the concentric layers, instead of a canal there is found one or more bone corpuscles."

A rough qualitative analysis of the material under examination showed large amounts of calcium and magnesium, some aluminum, a trace of iron, the carbonic, sulphuric, and hydrochloric acid radicals, and considerable organic matter. On complete incineration of a portion of bone in the oxidizing flame, reducing it to an amorphous white powder a loss of 17 per cent. by weight was noted. After heating until the mass charred and then lost its black color (becoming gray and not white as above and leaving no residue on solution with dilute hydrochloric acid) the percentage weight loss was on an average 10. Although the conclusions here are reached by a very rough method and are probably far from accurate, the 10 per cent. weight loss is taken to represent approximately the amount of organic matter and the additional 7 per cent. accounted for by the breaking up of the carbonates and the evolution of carbon dioxide. The source of the organic matter here is a question—whether remains of the original animal matter of the bone, or vegetable replacement during their stay in the soil. The latter possibility seems more reasonable and is supported by the finding of small roots in the medullary cavity of some of the bones sending their finer branchs into the cancellous structure and enlarged Haversian canals.

A description of the gross lesions of the bones is given here.

Specimen No. 1 ($\frac{1\,0\,6}{1\,0\,0\,0}$).* Complete right tibia which shows on its anterior and two lateral faces a large exostosis beginning about 3 cm. from the lower border of the tibial tubercle and extending down the whole length of the shaft to its junction with the lower epiphyseal portion. The joint surfaces are smooth and there are no periarticular projections. The exostosis is fusiform in shape and of such size as to result in a curving of the tibial crest with the con-

* The figures in parentheses refer to the Museum catalogue numbers of the Ohio State Archæological and Historical Society's collection.

vexity forward. Its surface is irregular and grooved with fine striæ each of which ends in an opening. The whole mass shows shallow, circumferential, wavy lines passing from behind forward and branching as they go. On longitudinal section the wall of the bone making up the exostosis is abnormally thick (1.5 cm.), and is made up of a layer of bone of slightly increased density (0.75 cm. in thickness), and of a mass of loose cellular construction encroaching on the medullary canal, which at one point is entirely shut off by a web-like mass of interwoven trabeculæ. The posterior wall of the bone is very slightly if at all affected either in thickness or density (to the unaided eye). The cancellous bone of the epiphyses is apparently unaltered.

Specimen No. 2 ($\frac{1}{1\,0\,0\,0}$). Left tibia (complete) showing slight curvature of the crest in the middle third of the shaft with a very smooth surface and few perforations. On the posterior surface at about the junction of the middle and lower thirds is an exostosis roughly ovoid in shape (4 cm. long by 3 cm. in width), sharply limited by the postero-external border, but extending for about 1 cm. on to the internal surface. This mass is smooth in its central portions, but grooved and perforated near its periphery and marked by one transverse furrow. On the internal aspect of the upper portion of the shaft at about the point of insertion of the sartorius, gracilis, and semimembranous muscles is an area of exceedingly rough contour and surface made up of numerous small, irregular, osteophytic growths. On the internal aspect and a little lower on the shaft in the origin of the tibialis posticus is another area with even more marked elevations and depressions, and surrounded by a zone in which appear numerous, closely arranged, narrow, parallel furrows, which appear as though they might have been the lines of attachment of fascicular bundles of connective tissue. Cross-section through the greatest prominence of the anterior curve shows very marked thickening of the bone forming the crest (2 cm.), which is very dense and was sawn with difficulty, in contrast to the fragility of most of the specimens. The epiphyses and articular surfaces appear normal and longitudinal section through the upper fourth shows no gross changes in the cancellous bone there.

Specimen No. 3 ($\frac{1}{1\,0\,0\,0}$). Right clavicle showing marked enlargement throughout its entire length with several small osteophytes at different points and an ill-defined exostosis on its superior surface just external to the junction of the two curves.

Specimen No. 4 (808). Left tibia, externally entirely normal in contour, surface, etc., except in the middle third of its shaft, which bears on its crest and the anterior part of its internal surfaces an exostosis 11 cm. long and raised, at its highest point, fully 1.5 cm. above the original crest. This growth is fusiform in shape, tapering off gradually to the normal size above and below. Its surface is smooth except where crossed in several places by vascular channels. Longitudinal and transverse sections through this bone revealed an intense hardness and a great thickening of the walls, which were for the most part very dense, but showed even in the most sclerotic areas various-sized intercommunicating cavities. Fig. 1 is a reproduction of a photograph of a cross-section of this bone through the exostosis compared with a cross-section of a normal (recent) tibia at a corresponding point on the shaft. The total width of this section from the crest to its posterior surface is 4 cm., of which 1.5 cm. is dense bone, 1.5 cm. cancellous tissue, and the remainder, 1 cm., medullary cavity. In this specimen although the external appearances gave no evidence thereof, the sclerosis and thickening were not confined to the exostotic area, nor to the anterior aspect, as all the walls were thickened and of increased density for almost the entire length of the shaft. Again, nothing abnormal was evident in the joints nor the epiphyseal cancellous structure. This specimen was most productive on microscopic examination, as will be shown later.

Fig. 1.—Cross-section through apex of exostosis of Specimen No. 4 (on the right) compared with a cross-section through a normal (recent) tibia at a corresponding part of the shaft. The exostotic section shows encroachment on the medullary cavity with thick sclerotic walls containing irregular porotic cavities. Four-fifths natural size.

Specimen No. 5 ($\frac{1\,0\,4}{1\,0\,0\,0}$). Fragment of upper end of left tibia, 9 cm. in length, showing very marked enlargement anteriorly, beginning at the tibial tubercle and extending down to the end. This growth gives the largest antero-posterior diameter of any of the bones at hand, *i.e.*, 5.5 cm., and its surface is scarred with minute pits and small osteophytes, vascular grooves, and the narrow furrows (origin of muscle bundles (?)) described in Specimen No. 2. The area of insertion of the popliteus is ridged and furrowed and the oblique line presents a tangled mass of osteophytes. The transverse section afforded by the broken end is pictured in Fig 2; it shows rarefaction to an intense degree, the worm-eaten spaces extending almost to the surface, and yet no evidence of an attempt at sequestrum formation. The smaller fragment in Fig. 5 is a view of the internal surface of this specimen and shows the roughness in the neigh-

borhood of the points of insertion of the sartorius, gracilis, and semimembranosus.

Specimen No. 6 ($\frac{103}{10000}$). Fragment of lower end of left tibia, 9 cm. long. Here is seen an exostosis covering the

FIG. 2.—View of end of fragment (Specimen No. 5) showing advanced osteoporosis, with encroachment on the medullary cavity by cancellous material. Four-fifths natural size.

internal face and extending on to the adjacent portion of the posterior. This is quite smooth, but marked by several branching bloodvessel grooves and through it, along the line of attachment of the interosseous membrane, runs a serrated ridge made up of irregular osteophytes. Cross-section of this fragment (Fig. 3) shows rarefying osteitis of

FIG. 3.—Cross-section of Specimen No. 6. Sclerosis was demonstrated in the wall. Porosis is evident in the gross appearance. Medullary canal almost filled with interlacing spicules. Five-thirds natural size.

the walls and a network of interlacing trabeculæ almost filling the central canal.

Specimen No. 7 ($\frac{107}{10000}$). Fragment of tibia consisting of one-half the upper articular surface and two-thirds of the shaft. This bone presents a very marked anterior curving which begins just below the tibial tubercle and extends to the end of the fragment. The posterior border is about normal, but the curve of the crest is so great as to give an anteroposterior diameter varying between 4 and 5 cm. The surface of this exostosis (the term seems proper here from the fact that all of the bone which remains above the line of the tubercle is unaltered) is lined with the fine, parallel vertical furrows, described above, but bears very few vascular grooves and no osteophytes. On cross-section the walls are thin, the marrow cavity is much enlarged, and there is a large amount of cancellous bone throughout the length of the shaft. This specimen is in contour very like the so-called "sabre-blade" deformity.* Fig. 4 is a photograph

FIG. 4.—Lateral aspect of upper 15 cm. of Specimen No. 7 (on the left) with a corresponding portion of a normal (recent) tibia (on the right) and a cross-section of each above. Two-fifths natural size.

of the upper 15 cm. mounted for contrast by the side of a corresponding part of a normal (recent) tibia and with a cross-section of each above its respective source.

* There is to be seen in the Smithsonian Institution a tibia taken from a mound in Butler County, Ohio, which shows involvement of the whole of the diaphysis. This exostosis gives rise to an anterior curvature of the crest similar to that described above, with the addition of deformity of the posterior border. The external surface of the internal malleolus is also involved. The joint surfaces of both epiphyses are normal. Cross-section afforded by an accidental recent fracture shows concurrent rarefying and condensing osteitis. The medullary canal is reduced to a thickness of about 0.5 cm., surrounded anteriorly by a mass of cancellous material, about 1 cm. in thickness, the remainder of the shaft, which is fully 6 cm. in its anteroposterior diameter, being made up of sclerotic material.

Specimen No. 8 ($\frac{100}{1000}$). Fragment of upper end of right tibia, 13 cm. in length. A portion of this bone amounting to about one-third of the full circumference and extending the full length of the fragment is lacking. The remainder presents much the same appearance as Specimen No. 5 with even more marked roughening of the oblique line by the osteophytic excrescences. (Fig. 5, large fragment.) The broken end of this piece shows a thin shell of hard bone encasing a layer of cancellous material except on the posterior edge where the dense bone is about normal in thickness. There is considerable enlargement anteriorly, and the outlines of the circumference is distorted to a rough ovoid shape.

Specimen No. 9 ($\frac{105}{1000}$). Fragment of shaft of tibia 5 cm. long and probably coming from about the middle of the diaphysis. Its external surface is rough and uneven, perforated by many small holes in some areas, marked by ridges and grooves in others, and on one side giving the impression that thin sheets of bone had been "plastered" on by the overlying periosteum. In cross-section it is ovoid and 4 cm. in its long axis. Anteriorly appears a wall of bone containing numerous communicating open spaces giving it a worm-eaten appearance. This is 0.5 cm. in thickness and is followed by 1.5 cm. of cancellous bone, then a marrow cavity 1 cm. in diameter, with rather definite walls from which bristle many very delicate interlacing spicules. About midway in the length of the central canal is a transverse septum of thin bone perforated by numerous small openings.

Fig. 5. Smaller fragment; lateral aspect of Specimen No. 5, showing anterior enlargement and rough, irregular surface at point of muscle attachments. (Fig. 2 is a view of the end of this specimen.)

Larger fragment—posterior aspect of Specimen No. 8, showing rough osteophytic excrescences on the oblique line and ridges in the area of origin of the tibialis posticus. One-half natural size.

Specimen No. 10 ($\frac{109}{1000}$). External cuneiform and third metatarsal bones firmly united by a complete bony ankylosis. The superficial layers of the cuneiform have been destroyed in places exposing the internal cancellous structures. The shaft of the metatarsal and its distal extremity appear normal and except for slight bony projections along the line of ankylosis there is nothing to suggest changes other than those which might arise from a traumatic or septic arthritis.

Considerable difficulty was encountered in cutting sections for microscopic examination. The final procedure adopted as productive of the best results was as follows: Rather thick sections were removed from the bone by means of a bracket saw and embedded in paraffin to allow of the cutting of narrower strips without destruction of the more delicate portions by crumbling. The paraffin was then removed by boiling on a flat sheet of metal, and the thin plates of bone were re-embedded and mounted on slides with Canada balsam, which had previously been boiled to remove the turpentine in order to give the proper consistence for the grinding which was done by means of files of varying degrees of coarseness. Grinding with whetstones, carborundum plates, pumice stone, and glass slides, and a variety of other things was tried, but without the success which followed the somewhat laborious task of filing.

Fig. 6.—Microphotograph of a portion of a section from Specimen No. 9, showing enlarged, irregular, and intercommunicating Haversian canals. This illustration is of an adjacent portion of the same slide as that shown in Fig. 7 and of the same magnification. Magnified 30 diameters.

Microscopic evidence was not needed to demonstrate the condition of rarefaction which was evident to the unaided eye in all the specimens. The demonstration of increase in density, however, required a more careful examination. In most of the sections the bone matrix appeared to be in an almost amorphous condition and showed little of the structure of the lamellæ or of the arrangement of the lacunæ and canaliculi, but even in these the size and shape of the Haversian canals was easily recognizable. Figs. 6 and 7

are microphotographs taken from the same slide which was a section of Specimen No. 9. These two pictures were of parts of the bone only a few millimetres apart, and show a marked contrast between the enlarged irregular communicating spaces of Fig. 6, which was in the line of the original bony wall and the dense structure with narrowed Haversian canals and areas with no apparent canal, which came from the compact part lying just beneath the periosteum. In this case the matrix was amorphous and the true arrangement of the lamellæ could not be made out. The specimen was deeply stained with gentian violet before filing to give contrast between the bone and the embedding balsam sufficient for the photograph.

Positive sclerosis was noted in specimens Nos. 1, 2, 4, 6, and 9. No sections were cut from Nos. 3, 5, 8, nor 10. No. 7, which was the tibia showing the "sabre-blade" deformity, gave no evidence of sclerosis. In nearly every case the

Fig. 7.—Microphotograph of an adjacent portion of the same slide from which Fig 6 was taken and of the same magnification; showing very marked narrowing of the lumina of the Haversian canals. Magnified 30 diameters.

sclerotic portion of the bone was its periosteal surface, the inner layers being porotic to an extreme degree.

One bone gave a picture which was in startling contrast to the structureless material of most. This one (No. 4) came from a mound at Chillicothe, Ohio, and its value in section was due to the fact that it had been infiltrated from its surface with a material later proved to contain iron, probably through the agency of the soil water. This was visible even to the naked eye as a dark staining, extending in from the surface and to some extent out from the medullary canal, and on section it showed as a deposit in the Haversian canals and in places even in the lacunæ and canaliculi giving an impregnated specimen. This enabled more careful study and showed some interesting conditions. Chemical tests of this bone showed that it contained quite an amount of iron, so a section was ground without the use of a file or other iron implements, and under the low power of the microscope the reaction in a slightly acid medium between the impregnating substance and a solution of potassium ferrocyanide was watched, as suggested by Dr. A. J. Smith, for this purpose, with the result that the deep color of Prussian blue appeared at first in the deposit, gradually spreading throughout the entire liquid. In view of the well-known preservative effects of the copper ornaments occasionally found with these remains it was suspected that possibly that metal might also be a factor with the iron in the impregnation, but all tests for it have proven negative.

In some parts of sections of this infiltrated bone is seen a microscopic picture which conforms closely with and at first was mistaken for the condition illustrated and described in Ziegler's *Pathology* as halisteresis ossium. The centre of bone trabeculæ in some fields was comparatively opaque and filled with more or less distinct lacunæ, while bordering the enlarged Haversian spaces was a facing of more translucent material. This condition is illustrated in Fig. 8.

Fig. 8.—Lighter layers of new-formed bone lying around enlarged Haversian canals and on the old trabeculæ. From a slide from Specimen No. 4. Magnified 350 diameters.

On closer examination, however, of this facing it was seen that it had a definitely laminated structure with fine cross-striations and some lacunæ and canaliculi. The relative scarcity of the lacunæ here is probably one factor in the difference in translucence, although the structure of the matrix itself is apparently also unlike that of the centre of the trabeculæ. To differentiate it still more clearly from osteoid tissue, its method of solution in dilute acid was watched under the microscope and the evolution of carbon dioxide was equally as rapid and voluminous there as in the adjoining portions. The cell spaces besides being fewer in number were considerably larger than their neighbors. Fig. 9 shows a microphotograph of two impregnated lacunæ with their canaliculi lying in these lighter layers. As an interpretation of this finding it is believed that this portion of the section represents an area where the change from cancellous material to sclerotic bone has just begun, that these lamellæ are the first of a new series to be laid down

on the old trabeculæ, and that the paucity of the cells and their size is an evidence of the changed conditions under which this new deposit was forming.

In other areas from these same sections, where the condensing osteitis had proceeded to a greater extent, were seen the outlines of old trabeculæ as marked by the arrangement of their lamellæ, and, within these, new Haversian systems lacking the normal symmetry of these structures and showing in many places the eccentric arrangement spoken of above in quotation from Cornil and Ranvier, and in several instances two complete systems within the outer lamellæ of a former. Here also were canals with their lumina almost or entirely obliterated.

A section of one of the thin layers of bone described in Specimen No. 9 as appearing as though "plastered" on by

Fig. 9. Infiltrated lacunæ and canaliculi from light layer of new-formed bone similar to that illustrated in Fig. 8 and from a slide of the same specimen. Magnified 400 diameters.

the periosteum proved that the canals here were perpendicular to the long axis of the shaft and to the canals of the bone beneath. This was also found in some of the osteophytic growths removed from lines of muscle insertion and origin, but in this case the arrangement was far from being so regular, and the canals were seen to cross and interweave in a promiscuous tangle.

Résumé. The material under examination is from a source undoubtedly pre-Columbian and the lesions are such as to justify the diagnosis of syphilis by the following pathological evidence: Changes affecting chiefly the diaphyses where long bones are concerned, showing a predilection for those bones which are most exposed to trauma, consisting of large exostoses and osteophytic overgrowths, and characterized by the concurrent presence in the same specimen of both a rarefying and condensing osteitis as demonstrated by gross and microscopic examination. Of 127 skeletons from one series of excavations, 21 showed traces of disease, 60 per cent. of the affected showed the changes most upon the tibia with the ulna, cranium, and sternum following in order. Of the specimens examined rarefying osteitis was grossly manifest in all but two, one of which (ankylosed metatarsal and cuneiform) was probably of traumatic or septic nature, and the other (a clavicle) was not examined in cross-section. Grossly sclerosis was evident in 3 of the 10, while on microscopic examination only 1 of 6 from which sections were taken failed to show condensation in some areas.

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References.

1. Buret, F. Syphilis in Ancient and Prehistoric Times. Translated from the French by A. H. Ohmann-Dumesnil, Philadelphia, 1895.

2. Astruc, John. De Morbus Venereis, libri novem, in quibus disseritur tum de origine, propagatione et contagione hornuce affectum in genere. Lutetiæ Parisiorum, 1740.

3. Bloch, Iwan. Der Ursprung der Syphilis Jena, 1901. Der Erste Auftreten der Syphilis (Lustseuche) in der Europaischen Kulturwelt, Jena, 1904.

4. Jones, Joseph. Exploration of the Aboriginal Remains of Tennessee; Smithsonian Institution Report, Washington, 1876. Exploration and Researches Concerning the Destruction of the Aboriginal Inhabitants of America. New Orleans Medical and Surgical Journal, June, 1878.

5. Brühl, Gustavus. On the pre-Columbian Existence of Syphilis in America, Cincinnati Lancet-Clinic, May, 1880, and March, 1890.

6. Hyde, James Nevins. A Contribution to the Study of pre-Columbian Syphilis in America. American Journal of the Medical Sciences, August, 1891.

7. Lang, Edward. Twentieth Century Practice of Medicine, New York, 1899.

8. Hyde and Montgomery. Syphilis and the Venereal Diseases, Philadelphia, 1900.

9. Le Baron. Thèse de Paris, 1881; quoted from Buret (Reference No. 1).

10. The American Text-book of Genitourinary Diseases, Syphilis, and Diseases of the Skin. Philadelphia, 1898.

11. Cornil and Ranvier. Manuel d'Histologie Pathologique. Paris, 1881.

12. Lazarus-Barlow, W. S. Pathological Histology and Anatomy, Philadelphia, 1903.

13. Cornil. Syphilis. Translated from the French by J. H. C. Simes and J. William White. Philadelphia, 1882.

14. Cornil and Ranvier. Pathology. Translated from the French, with notes and additions, by E. O. Shakespeare and J. H. C. Simes. Philadelphia, 1880.

STUDIES ON CELL GRANULA AND AMŒBOID MOVEMENTS OF THE BLOOD CELLS OF LIMULUS.

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As much as granula and other cell structures, especially of blood cells, have been studied in fixed and stained specimens, relatively little is known in regard to their behavior in the living cells. The following is intended as a contribution to the study of cell granula from a physiological rather than from an anatomical point of view. The granula are examined in their connection with the amœboid movements of the cell and under various experimental conditions.

In selecting a promising material for these investigations the large amœboid blood cells of invertebrates, as, for instance, of Limulus, were considered more favorable than the leukocytes of vertebrates. The conditions determining the structural characters of the blood cells of vertebrates and invertebrates are not identical, and this fact will have to be considered in applying the following results to vertebrate and especially to mammalian blood cells. At present we may, however, assume that some of the more essential features are common to both kinds of cells.[1]

In former investigations the influence of the blood cells of Limulus upon the coagulation of the blood and their behavior under inflammatory conditions were studied. It was found that the blood cells could be transformed into masses resembling fibrin, and that under the influence of certain mechanical conditions structures could be produced which showed many analogies to connective tissue. The behavior of the blood cells which had left the body of the animal was on the slide similar to the changes which are produced in leukocytes inside the body of the animal in inflammatory processes. Under these conditions the blood cells of Limulus agglutinate.

In the following investigations the influence of certain mechanical and chemical conditions upon cell structures, especially upon the granula and also upon amœboid movements and upon the consistency of the cell, was investigated.[2]

The experiments were made in the following way: A moist chamber was prepared by covering a small dish containing water with a large bowl. Two very clean slides were put on the dish. The solution, the influence of which upon the blood cells was to be investigated, covered the surface of the slides. The blood was taken from animals from about one to two months old. In the beginning of the experiments a cut was made with a scalpel into the dorsal joint of the animal. Later a clean trocar was pushed into the heart, and in the last experiments the trocar was oiled before the blood was withdrawn. If possible one drop of blood was received on the centre of the slide, so that in each experiment approximately the same amount of blood was mixed with the same quantity of solution.

In several experiments the quantity of solution used was increased up to 100 c.c., with which a bowl was filled. The slides which were to receive the blood were suspended in the upper parts of the solution. In this way the influence of the substances present in the blood plasma was considerably decreased. Before each microscopic examination of the blood, the greater part of the solution was carefully removed from the slide; after the observation had been made the slide was sometimes covered with fresh solution if a later observation of the same specimen was desired. Usually two slides were covered with the same solution in each instance, so that it was possible to examine the influence of the same solution at different periods. In the majority of cases the observations were made one to three hours after the blood had been withdrawn. In many cases, however, observations were made at earlier or later periods.

Certain irregularities in the results were sometimes caused by the fact that the amount of blood received upon a slide was not the same in all cases. It happened not rarely that more than one drop was added to one slide. Furthermore, the blood did not always flow with the same rapidity from the animal, whether or not a cannula was used. That depended upon whether or not the heart of the animal had been extensively opened. It was also of importance how much of the inner side of the metal cannula was smooth. As we shall see later, a foreign body which is not quite smooth causes changes of the blood cells, whereby the cells become more sticky. We therefore find that the blood flows much more rapidly through a cannula that has been oiled previously than through one which has not been

[1] A review of the more important literature on cell granula is given in Ehrlich and Lazarus' "Die Anæmie," Nothnagel's specielle Pathologie and Therapie.

[2] The changes of the blood cells which take place apparently spontaneously in the blood which has been withdrawn from the animal have been descibed in two earlier papers: "On the Blood-lymph Cells of Limulus," etc., Journal of Medical Research, January, 1902, vol. vii., No. 1, and Virchow's Archiv, 1903, vol. clxxiii. In these papers the literature on the subject is given. It is intended to continue these investigations next summer.

oiled. This probably is caused principally by the increased adhesion of the blood cells passing over the surface of the cannula. It happened that the blood coagulated already inside the cannula on its way to the slide in cases in which the interior of the cannula contained small foreign bodies, as, for instance, particles of dust. Further variations were caused by the different height from which the blood fell upon the slide. The difference in the surface tension of different solutions which covered the slide may also have been of some importance. The breaking through the surface layer of the solution had a certain mechanical effect, which caused a change in a number of blood cells.

In the blood which passes through the cannula very slowly, changes may take place before it reaches the slide. Only those experiments have been included in the following notes in which the above-mentioned sources of error have been avoided as much as possible.

Three sets of factors influence the behavior of the blood cells:

1. The mechanical effect of the passage through the frequently narrow wound or of the breaking through of the surface layer of the solution covering the slide and the mechanical shock caused by the blood falling upon the surface of the slide.

2. The influence of the solid body with which the blood cells come into contact after they have been mixed with the fluid covering the slide.

3. The influence of the solution in which the blood cells are suspended. This solution influences the blood cells (*a*) by its osmotic pressure; (*b*) by its reaction (quantity of H or OH ions), and (*c*) by the chemical character of the dissolved substances (the factor named under (*b*) excluded).

If we cut with a fine scalpel through the dorsal joint into the heart of a small Limulus and receive a drop of blood upon a clean slide, we find under the microscope all those changes of the blood cells which I have described in previous papers. The large majority of the cells are changed. Granula are lost. Protoplasm flows out from the cells. Many cells show the so-called explosive disintegration. The large majority of all cells become round in a very short time and send out pseudopodia in the next few minutes. Many cells are drawn out into fibres, so that we soon find a network of fibres and cells crossing the drop of blood in all directions. If, on the other hand, we withdraw the blood through an absolutely clean metal cannula from the heart of the animal through the dorsal joint and receive a drop upon a clean slide, we find under the microscope an absolutely different picture. The large majority of the blood cells, which are well preserved, have an oval to round shape. All or almost all granula are present. The cells are either free or stick to each other only loosely, without being connected by threads. No pseudopodia are formed. Gradually the blood cells sink down to the surface of the slide. The supernatant fluid remains clear and movable. In successful experiments, in which all requirements in regard to the cannula, withdrawal of the blood, and slide had been fulfilled, the fluid does not contain any threads and can easily be poured off. The blood cells which have arrived upon the surface of the slide gradually begin to spread out by sending out blunt pseudopodia. Under these conditions granula disappear only very slowly and the cells can spread out in an amœboid way for considerable time, and, notwithstanding this, may retain the large majority of their granules. Gradually, however, even under these circumstances, a large number of granules disappear in the cells which are spread out. On the other hand, the cells which are suspended in the lower parts of the blood plasma, and which are separated from the surface of the slide by a layer of spread-out cells, retain either a round or oval shape and do not lose their granula. Not rarely however, it happens that in those cells which are suspended very near the surface of the slide, a few small pseudopodia are formed, usually on both sides. These pseudopodia in every case turn downward toward the glass, and if they touch the surface of the slide they stick to it. Under these conditions pseudopodia are never directed upward.

In one experiment, for instance, the blood of a grown-up Limulus had been received through a cannula upon two slides. Immediately after the drop had fallen upon the slides almost all the blood cells were unchanged. Soon, however, a very large number of the cells sank down to the bottom. The large majority of the cells preserved their elliptic or oval shape. After seven and one-half minutes the large majority of the cells lying on the surface of the glass are still normal; only a few cells are changed. After ten minutes one of the two slides covered by the blood was moved up and down several times. This movement was sufficient to change many cells, as a microscopic examination showed. Masses of granules are seen outside of cells. Many of the cells appear as if they had been broken up and had flown into the surrounding liquid. On the other slide, which had been kept quiet, the cells were well preserved after fourteen minutes. Many, however, appeared round, although a certain number had preserved their oval shape. After twenty-four minutes the cells in contact with the glass spread out and formed a network. From these spread-out cells many granula disappeared gradually. In another experiment the round to oval cells containing granula sent out hyaline pseudopodia laterally downward after one hour. It is, however, possible that such a change takes place after thirty-five minutes.

Similar results are obtained if we collect a large quantity of blood from a grown Limulus into a larger bowl. Blood which had been obtained by a mere cut into the large ventral vessels forms a gelatinous mass, in which the cell protoplasm forms threads, which pass through the fluid in all

directions. If, on the other hand, we collect the blood in a glass bowl through a clean, metal cannula from the heart,[1] it is possible to avoid the formation of threads. The cells sink gradually to the bottom just as they do under similar conditions on the slide. The supernatant fluid can be poured off. The microscopic examination shows that the cells obtained under these conditions remain just as well preserved as the ones obtained on a slide through a cannula. If, however, sea-water or even distilled water is poured into the bowl which is intended to receive the blood, the latter behaves as if it had been obtained without a cannula. Two factors may account for this result:

1. The breaking through the surface layer of the fluid which is in the bowls. It is probable that this mechanical factor is of some significance, because we may find in the upper parts of the blood some rows of changed cells which do not contain any granula, even if we allow one drop of blood to fall upon another drop of blood.

2. The chemical constitution of the surrounding fluid changes the cells in such a way that the granula are lost and cellular threads are formed. It is intended to discuss the latter factor later on.

If, however, one collects very cautiously in a large surplus of distilled water a small quantity of blood flowing out of the animal very rapidly, so that the blood is equally distributed in the water, it is possible that many swollen cells sink to the bottom of the vessel without having formed threads. On the other hand, certain chemical changes in the fluid in which the cells are suspended may alone be sufficient to produce such changes in the cells that the protoplasm is transformed into threads. This can be shown by the fact that if we inject sea-water into the heart of a Limulus the blood is transformed into a gelatinous mass inside of the animal body. If five to ten minutes after an injection of about 5 to 7 c.c. sea-water in the heart of an adult Limulus the heart of the animal is opened as rapidly as possible, the blood in the heart is found to be more or less coagulated. After injection of distilled water this result is not as constantly obtained. Where the needle has pierced the vessel wall a local coagulum is formed. We see, therefore, that mechanical influences, consisting in the passing of the blood through a narrow, uneven wound in the soft tissue and in the chitinous wall, change the blood cells in such a way that soon after they have fallen upon the glass or have mixed with the fluid present in the bowl, and partially perhaps already before they have reached the glass or the fluid, all those changes take place which have been described, leading to the formation of pseudopodia, to a loss of granules, to an explosive disinintegration, and to the formation of threads, and in this way a gelatinous mass is produced.

It is to be considered whether the action of the passing through the wound is merely a mechanical one or whether a specific action of the coagulins present in the muscle and in other tissues is at work. The latter factor is improbable for the reason that so far it has not been possible to demonstrate in the blood of Limulus fibrinogen coagulable under the influence of tissue coagulins. If we receive the blood through a cannula in a dish in which the muscle extract of Limulus or of a lobster is present instead of in a bowl containing sea-water, we find the blood to behave in both cases in the same way. It is, therefore, very probable that in each case changes in the cell protoplasm are merely produced by mechanical factors, or by the chemical constitution of the liquid differing from the constitution of the blood plasma without specific influences of the tissue coagulins being in this case of any significance. These mechanical or chemical factors cause the change in the shape of the blood cells and make them sticky and lead directly or indirectly to a loss of many granules. That mechanical influences are able to cause the explosive disintegration of cells can be demonstrated in a drop of blood containing well-preserved cells lying on the surface of the slides by moving the slide rapidly up and down. In this case many cells are broken, so that the granula are widely spread out.

The cannulas used in these experiments being usually not absolutely free from dust or moisture, frequently a large number of cells are changed. Others perhaps are changed as a result of the shock caused by the falling of the drop upon the slide, and we therefore see that in the upper layers of the blood, even when obtained with all precautions, threads composed of a number of cells without granula and possessing pseudopodia are present.

If we avoid to a great extent the influence of the above-named mechanical factors and of the chemically changed fluid, by receiving the blood through a clean cannula directly on the slide, the second factor comes into play, namely, the contact of the cells with the glass, or perhaps even the influence of the close proximity of the glass. We see that the cells, which were round or oval as long as they were suspended in the fluid, begin to spread out as soon as they touch the glass, or that they send out pseudopodia even as soon as they are near the glass. Haycraft and Carlier[1] had already made the observation that in crab blood collected in oil the cells do not show any amœboid movements.

If we withdraw the blood of a Limulus through an oiled cannula and collect it in pure olive oil, the result is essentially the same as if the drop of blood is received through a pure metal cannula on a clean slide. Only those blood cells which come into contact with the glass send out pseudopodia, spread out, and become so sticky that they adhere to the glass. In oil the number of cells which come into contact with the glass is, however, smaller than in the drop of blood which

[1] I am greatly indebted to Dr. Carlson for his aid in obtaining the blood directly from the heart of Limulus

[1] On Invertebrate Blood Removed from the Vessels and Entirely Surrounded by Oil, Proceedings of Royal Society of Edinburgh, vol. xv.

is surrounded by air, the rounded form of the drop of blood being better preserved in oil than in air. In one experiment, for instance, the cells in the drop of blood surrounded by oil were still round to oval after fifteen to thirty minutes. The granula were present. Almost all the cells were well preserved. In a few cells some granules had been dissolved. At the surface of the drop only a few threads were visible, which were composed of hyaline cells joined to each other by their processes. After one-half hour the cells, with many well-preserved granula, were widely spread out on the surface of the glass. All other cells, however, which were suspended in the fluid were without processes, and only a few cells had been transformed into masses of granula through mechanical shock. Oil itself is apparently an indifferent substance in regard to blood cells. It is, however, possible that the round or oval cells agglutinate even in oil, so that macroscopically the formation of threads and therefore the appearance of a coagulation is not necessarily entirely avoided. Haycraft concludes from his experiments that a solid body incites the blood cells to amœboid movements. The wall of the bloodvessel, which is also solid, does, however, not have any such effect upon the blood cells, and therefore we may perhaps assume that it depends upon the character of the solid body. It might perhaps contribute to the understanding of these facts if we assume that lipoid substances are very important constituents of the cell, and that according to Overton and H. Meyer especially the outer layer of the cells behaves like a lipoid substance. That would explain why the intact endothelium of bloodvessels behaves similarly to oil. Very smooth metal surfaces do not produce such pronounced changes in the blood cells as uneven surfaces do. That is proven by the fact that the collecting of the blood through a clean metal cannula leaves the blood cells in the main unchanged and that, on the other hand, the presence of rough substances inside the cannula produces pronounced changes in the cells.

It might be of interest to examine in some future investigations what other factors are of importance in determining the effect of solid bodies upon cells.

As soon as the blood cells begin to spread out in contact with the glass, many granules of the cells which are spread out become lost. The rapidity with which this takes place is not always the same. Usually a large number of granules remain intact for a longer period, even in those cells which have spread out in an amœboid way. There is a marked difference, however, between the contracted cells which are suspended in the blood plasma and the spread-out cells on the surface of the slide. In the former usually almost all the granules remain unchanged. In the latter they dissolve to a great extent. We find a similar difference in the behavior of these cells if we collect the blood cells in a number of solutions which are able to dissolve the granules. We also find that the contracted cells preserve their granules much longer than the cells which are spread out. This fact suggests that in the latter cells the granules are more accessible to the dissolving influences of the surrounding fluid than in the contracted cells. The spreading out of the cells would therefore be in this case only an indirect cause of the dissolution of the granules. It might, however, very well be possible that the same conditions which change the shape and produce the stickiness of the cells have also a directly dissolving influence upon the granules.

If it is possible by using all these means to preserve the blood cells in an almost unchanged state outside of the body, the process of withdrawing the blood itself is nevertheless sufficient to produce a certain change of shape of the cells. If we observe the blood cells in a cut-out gill plate, a large number of the cells appear not only as oval but as quite flat, almost disk-like cells. If, however, we withdraw the blood from the body even through a cannula which had been oiled, we see, instead of flat, disk-like cells, oval to round cells, which have become somewhat sticky, so that the neighboring cells may agglutinate.

After having analyzed the cell changes which are produced by mechanical circumstances and through solid bodies, we are able to explain all other changes through the influence of the surrounding fluid.[1]

The osmotic pressure of the sea-water corresponds approximately to a $\frac{5}{8}$ m. sodium chloride solution. The osmotic pressure of the blood of arthropods is very similar to sea-water. The same sodium chloride solution corresponds, therefore, approximately to the osmotic pressure of the blood. If we collect a drop of blood in such a salt solution the cells which are in contact with the slide send out amœboid processes, but even the majority of the cells which are suspended in the liquid send out processes within a short period. A few cells preserve their round shape for a certain time. The body of most of the cells is slender. Long pseudopodia are drawn out. The large majority of the granules are soon lost. Processes of the different cells anastomose with each other. Gradually a network is produced in the solution, inasmuch as rows of cells come into closer approximation to each other, probably as a result of the elastic retraction of the cell threads. In a similar way the cells behave in sea-water. If we receive the blood upon a slide which is suspended in the upper parts of a bowl filled with 100 c.c. of sodium chloride solution, the behavior of the cells is similar. The pseudopodia, however, are somewhat smaller under these conditions and the cell body somewhat more round. In a large quantity of sea-water the blood cells show the same changes as the ones seen in a small amount of sea-water on the slide. The same effect is produced by 100 c.c. of a $\frac{5}{8}$ m. NaCl solution to which about 5 c.c. to 10 c.c. of a $\frac{5}{8}$ m. $CaCl_2$ solution has been added. The larger the amount of

[1] In most cases Kahlbaum's and in a few experiments Merck's preparations were used.

fluid by which the drop of blood is surrounded, the smaller is the significance of the substances which are contained in the blood plasma itself.

Hypertonic Solutions. If instead of a $\frac{5}{8}$ m. NaCl solution we use a $\frac{5}{4}$ or $\frac{4}{4}$ m. NaCl solution, a delay takes place in the development of all those processes which take place in a $\frac{5}{8}$ m. NaCl solution. After a longer period, however, the typical formation of pseudopodia takes place in this solution, and a network of cells, which are mostly without granules and very slender, is produced. In a 2 m. NaCl solution the formation of pseudopodia does not take place and the majority of the granules remain preserved. The cells maintain their round shape. Frequently, however, they are deformed, and it is not possible to distinguish the individual granules. The cells can be still drawn out with the aid of a needle several hours after they have been mixed with the fluid. After two hours and a quarter it is, for instance, possible to draw out by means of a fine needle a cell into a surprisingly large mass of granules which are connected by protoplasm.

In a 4 m. NaCl solution the large majority of the cells preserve more or less their oval shape. The cells, however, may shrink somewhat. Their granules remain intact. In this solution it is no longer possible to transform the cells by means of a needle into large masses of granules. The cells have been hardened too much. It is, however, possible to transform the cells into small plates containing many small parallel fibrils with granules by exerting an even pressure upon them with a needle gliding over their surface. The cells behave in a similar way in a 3 m. NaCl solution. Here also they are not very sticky and are not very easily changed by mechanical agents. A 2m. NaCl solution is, therefore, able to withdraw water from the cells, and in this way to prevent the dissolution of the granules and the spreading out of pseudopodia. A 4 m. NaCl solution acts much more intensely. In this solution so much water is withdrawn from the outer part of the cells that not only are the granules preserved and the sending out of pseudopodia prevented, but that even the oval and disk-like shape of the cells remains approximately preserved.

In a 40 per cent. urea solution the granules mostly disappear. The cells are oval and cannot be easily drawn out by a needle. A 28 per cent. urea solution is not able to prevent changes of the cells by its osmotic pressure. Around the central part of the cell, which in the beginning may still contain granules, a large, swollen, hyaline zone is formed, which by the aid of a needle can easily be drawn out into fibres.

Hypotonic Solutions. If we collect a drop of blood in distilled water pseudopodia are not sent out. The granula disappear. The outlines of the cells and frequently also of the nuclei are often sharply defined. It is easily possible to draw out the cells into threads. A 0.5 per cent. ($\frac{m}{11}$) NaCl solution makes it only possible for the centrally situated cells to send out pseudopodia and to form a network, because in the central part of the blood the osmotic pressure of the plasma increases the osmotic pressure of the solution. Peripherally situated cells behave as in distilled water. The concentration of the fluid which is necessary for the formation of pseudopodia is, therefore, somewhat higher than corresponds to a 0.5 per cent. sodium chloride solution if we use this salt. In a 1 per cent. sodium chloride solution we find the typical formation of a network of hyaline cells which have sent out pseudopodia. In other salt solutions, however, the osmotic pressure permitting the formation of pseudopodia differs somewhat from that of a sodium chloride solution, as we shall see later.

Reaction of the Solution. Strongly alkaline or acid solutions prevent the sending out of pseudopodia. Pseudopodia can only be formed if the reaction is neutral or very weakly alkaline. Granula remain preserved if the reaction is alkaline, provided the alkalinity is not strong enough to cause the swelling and disintegration of the whole cell. The granules remain preserved also, if we use very weak acid solutions, as, for instance, a $\frac{1}{8}$ m. solution of NaH_2PO_4. They are, however, lost under the influence of a somewhat stronger acid. In $\frac{5}{8}$ m. NaH_2PO_4 the cells remain well preserved and round. The granules are not dissolved. The consistency of the cells is soft. The same takes place in $\frac{5}{8}$ m. KH_2PO_4 and in $\frac{5}{16}$ m. KH_2PO_4. In $\frac{5}{8}$ m. Na_2HPO_4 many granules are lost and a number of pseudopodia are formed. The number and size of the pseudopodia are, however, smaller than in a $\frac{5}{8}$ m. NaCl solution. The cells do not form a network as they do in the latter solution. In $\frac{5}{8}$ m. $NaHCO_3$ almost all the cells remain oval, and the granules are well preserved, provided the experiments are successful. The cells are frequently drawn out at both ends in thin threads, by which they are connected with each other. Many rows of cells formed in this way may be closely attached to each other, so that a network is formed. No pseudopodia are sent out. Sometimes, however, probably if the quantity of the added blood was too much or if changes took place at the time the blood was withdrawn, at least a part of the granules are lost and a very slight formation of pseudopodia, which are directed toward the surface of the slide, may be observed. If the alkalinity becomes more marked the changes in the cells present in the solution are much greater. In $\frac{1}{2}$ m. Na_2CO_3, we see, for instance, after eighteen minutes, large, swollen, round to oval cells without processes. The cells are hardly visible and apparently contain fine granules. The quantity of the precipitate formed makes the determination of the exact character of the granules difficult. If we collect a drop of blood in a solution of a mixture of 5 c.c. of a $\frac{5}{8}$ m. KCl solution and 5 c.c. of a $\frac{1}{5}$ m. NaOH solution, many cells with their granules remain well preserved for some time. Other cells, however, form large, swollen, hyaline balls. If we now add fresh solution at a

place where large masses of well-preserved cells are lying, it is possible to observe under the microscope how many cells gradually swell, as if imbibing water, and how they suddenly rupture at one place. The granules remain preserved. They are attached to the surface of the cell. If, however, the liquefaction of the protoplasm proceeds still further, the granules may become entirely free.

Under the influence of a somewhat stronger acid, for instance, of a mixture of 12 c.c. of a $\frac{5}{8}$ m. KCl solution and of 5 c.c. of a 0.5 per cent. HCl, the cells become hyaline, preserving an oval or round outline. The contours of the cells are smooth and very sharply defined. In the same way the outlines of the nuclei are very distinct. In the nucleus granules are frequently visible. Even in acid solutions, it may, however, happen that a part of the granules remain preserved. Such variations probably depend upon the quantity of the blood upon one slide, which may make it possible for only a certain amount of acid to act upon the cells, the rest of the acid being, perhaps, made inactive by combining with proteids of the plasma. If in such a case we add a fresh amount of a 0.5 per cent. HCl solution, we may observe that in some cells one granule after the other rapidly disappears. Under these conditions the cell swells somewhat, becomes oval and transparent, and the nucleus is very distinct.

Influence of Other Constituents of the Solutions. (*a*) *Non-electrolytes.* In isotonic solutions of urea and glycerin the cells do not form pseudopodia. A network of cells possessing pseudopodia is not produced. If, however, a $\frac{1}{3}$ m. solution of urea, instead of a molecular solution, is used, it is possible that the cells lying in the periphery of the blood drop lose their granules, send out pseudopodia, and form a hyaline network. In this case the osmotic pressure of the blood plasma is sufficient to make possible the formation of pseudopodia and of a retracted network of cells. The same may take place in a molecular glycerin solution, if we use much blood and relatively little glycerin. In solutions of urea and glycerin the granules disappear gradually. A number of granules, however, may be preserved during a certain period. Even more concentrated solutions of glycerin and urea are not able to preserve the granules.

In a 40 per cent. solution of urea, which is almost a seven times molecular solution, the cells may preserve their oval shape. They become hard and cannot be easily drawn out into threads. In a 20 per cent. solution the cells are soft and can be drawn out into threads. In both cases the nuclei have frequently the shape of rods. We therefore find the osmotic pressure, which is able to preserve the shape of the cells about equal in solutions of urea and of NaCl. In solutions of urea which are isotonic with blood, the nucleus is usually clearly visible, and its contours are sharply defined. The cell is either round or has a wavy outline. The outer parts of the protoplasm are hyaline. In solutions of glycerin which are isotonic with blood the nucleus is very well visible, and the outlines of the protoplasm are frequently sharply defined. The cells are soft and can easily be drawn out into threads. In somewhat stronger solutions of urea, for instance, in 2 m. solutions, it is frequently possible to observe a swelling of the nucleus of the cell protoplasm, so that the cells may be connected by swollen masses of protoplasm, which are almost invisible.

We see, therefore, that molecular urea and glycerin solutions behave essentially in a similar way toward the blood cells as distilled water; especially in urea the cells may, however, swell, even in hypertonic solutions.

Isotonic solutions of cane-sugar or glucose act somewhat differently. In these solutions the cells lose their granules also. The protoplasm of the cells becomes very homogeneous without showing any differentiations. The cells, however, frequently send out pseudopodia, and many cells are packed so densely together that the limits of the individual cells are frequently not visible. The cell masses may be connected by cellular threads. We see, therefore, a difference in the behavior of solutions of glycerin and urea on the one side, and of sugar solutions on the other side. This difference is perhaps caused by the fact that, according to Overton, urea and glycerin penetrate more easily into cells than do solutions of sugar.

(*b*) *Electrolytes.* Different from the solutions of these non-electrolytes, behave solutions of salts which are isotonic with blood. If we compare isotonic solutions of salts with each other, we find that the different salts act differently. It is possible to show constant differences between elements which, like sodium and potassium, are nearly related to each other in the periodic system. The influence of a $\frac{5}{8}$ m. NaCl solution has been described previously. Slender cells without granules, with long pseudopodia, form a very strongly retracted network. In the beginning some granules may be preserved inside of the cells; especially round cells suspended in the fluid may preserve their granules for a certain period.

In a $\frac{5}{8}$ m. KCl solution the cells behave somewhat differently. If the blood was collected under favorable conditions (very clean metal cannula, rapid flowing out of the blood from the heart, and small quantity of blood mixed with the fluid), the cells differ from the cells which were received in an isotonic NaCl solution in the following way: First, the cells in the KCl solution do not form a retracted network as can be seen in a $\frac{5}{8}$ m. NaCl solution, but they are more equally distributed in the fluid. Second, the granules are better preserved. Third, the cells differ in their shape from the cells in a NaCl solution. The number of round to oval cells containing granula and not spreading out, but suspended in the fluid above the slide, and frequently agglutinating with each other, is much greater than in a NaCl solution. Furthermore, even the cells which spread out upon the surface of the slide preserve their granules much better than they do in an isotonic NaCl solution. The

spread-out cells are flatter and not as slender as in a NaCl solution. Their processes are not as pointed, but more blunt. Gradually, however, the round cells containing granula spread out more and more, and slowly many granules of the spread-out cells disappear, just as we see in a drop of blood which has been collected upon a dry slide. After one hour most of the cells may still be round to oval, sometimes sending out small hyaline pseudopodia on both sides in the direction toward the glass. We may observe the same phenomena in blood cells which have been collected in a $\frac{1}{2}$ m. KCl solution. Certain changes in the blood cells, however, can in both cases take place earlier; for instance, after twenty-five minutes. We may also observe in the KCl solution in the upper parts of the fluid some rows of hyaline cells, which have probably been formed under the mechanical influence of the breaking through the surface layer of the fluid. If we compare the behavior of the blood cells in a NaCl and a KCl solution and in a drop of blood which was received on a dry slide, we find the great similarity in the behavior of the cells in a $\frac{5}{8}$ m. or a $\frac{1}{2}$ m. KCl solution and in the blood plasma. On the other hand, the cells behave very differently in the blood plasma and in a $\frac{5}{8}$ m. or a $\frac{1}{2}$ m. NaCl solution. The difference, however, between the effects of a $\frac{5}{8}$ m. KCl solution and a NaCl solution is not so pronounced in each instance. If the blood cells were injured during the process of withdrawing the blood, we may see, even in a KCl solution, very many cells without granula sending out hyaline pseudopodia. The behavior of the cells may then, under certain conditions, be similar in a KCl and in a NaCl solution. We are, however, always able to demonstrate the difference in the action of a NaCl solution and a KCl solution in two ways: First, if we use diluted solutions—for instance, if we use a $\frac{1}{4}$ m. solution instead of a $\frac{1}{2}$ m. solution—the difference between NaCl and KCl is always quite distinct. In a $\frac{1}{8}$ m. KCl solution most of the cells are round to oval and are swollen. The nucleus is frequently swollen and granular. The cells are almost without processes, or form only one blunt process. They do not form a retracted network. In a $\frac{1}{8}$ m. NaCl solution on the other side the behavior of the blood cells is not very different from that which is seen in a $\frac{1}{2}$ m. NaCl solution. In both cases we find a network of hyaline, slender, drawn-out cells, which have pseudopodia. Secondly, the difference can also be demonstrated if we add to one part of a $\frac{1}{2}$ m. NaCl or KCl solution one or two or even four parts of a molecular glycerin or molecular urea solution. In a solution which consists of two parts of a molecular urea solution plus one part of a $\frac{5}{8}$ m. KCl solution, the cells are all round and frequently possess granula, part of which may disappear. The cells do not form pseudopodia and are not arranged in a network. On the other hand, in a mixture of NaCl and urea solutions, we find cells possessing pseudopodia. The cells are arranged in the form of a network. The influence of the urea in this mixture becomes perhaps apparent through the somewhat smaller number of pseudopodia and through the presence of some round cells, the number of which is somewhat larger than in a pure NaCl solution. The same holds good of combinations of glycerin and salts. Here also the cells and the nuclei of the salts swell in a mixture of a KCl solution and of glycerin. We may conclude that the NaCl solutions are much more resistant toward dilution with water or with urea and glycerin than the KCl solutions. The former are more antagonistic toward the action of water, glycerin, or urea upon the blood cells than KCl solutions.

The addition of $\frac{1}{2}$ c.c. of a $\frac{5}{8}$ m. NaCl solution to 2 c.c. of a molecular urea solution is sufficient to cause the net-like arrangement of the cells and the formation of pseudopodia to appear. These changes may not be as marked as if a larger amount of NaCl solution is added.

If we use instead of an isotonic a molecular KCl solution, we find after the first hour that the result is similar as if a molecular NaCl solution had been used. The spreading out of the cells is retarded. Cells collected in a molecular KCl solution can just as well be drawn out into large masses of granules as cells collected in a molecular NaCl solution.

The same difference which exists between KCl and NaCl solutions can also be demonstrated between other Na and K salts. It exists between KBr and NaBr, between KNO_3 and $NaNO_3$, between K_2SO_4 and Na_2SO_4. In the case of these salts, again, the difference is clearer if we use more diluted solutions. For instance, if we use $\frac{1}{8}$ m. instead of $\frac{1}{2}$ m. solutions, or if we use in the case of the sulphates $\frac{1}{16}$ m. solutions, taking into account the higher osmotic pressure exerted by solutions of sulphates, the character of the cells in the above-named K and Na salt solutions is, on the whole, the same as in the corresponding chloride solutions. The influence of the *anion* is very small in these cases. We find, however, that a $\frac{1}{2}$ m. $NaNO_3$ does not show the influence of the Na as much as a $\frac{1}{2}$ m. NaCl solution. In a $\frac{1}{2}$ m. $NaNO_3$ solution the cells are very frequently similar to the cells in solutions of KNO_3 and KCl. Certain differences in the character of the cells, however, show the influence of the *cation* in a $NaNO_3$ solution. In $\frac{5}{8}$ m. K_2SO_4 and Na_2SO_4 solutions the cells present a similar appearance as in a molecular NaCl solution. This fact is presumably, in part, at least, caused by the hypertonic character of the solutions, and not by the specific effect of the SO_4. A certain difference exists, however, between a K_2SO_4 and a Na_2SO_4 solution. In the former more granules are preserved, and a smaller number of pseudopodia are formed. In $\frac{5}{8}$ m. NaI and KI solutions the cells remain well preserved, the granules are present, and only few pseudopodia are formed. This is presumably caused, in part, at least, by the presence of free iodine in these solutions. In a $\frac{1}{2}$ m. NaF solution the cells remain round to oval, and most of the granules disappear. A few granules around

the nucleus may, however, be preserved. The nucleus itself may appear granular. NaF acts, therefore, very differently from other sodium salts.

The chlorides of other alkaline metals act in the following way:

LiCl acts almost like NaCl. In $\frac{1}{2}$ m. CsCl, we do not find the net-like retraction of the cells which we find in NaCl solutions. The cells are mostly round, and only few pseudopodia are formed. Frequently the nucleus in the centre of the cell is very clearly visible. In its periphery we find swollen granules, which are probably in the process of dissolution. The contour of the cell is not distinct. In $\frac{1}{2}$ m. RbCl the behavior of the cells is somewhat intermediate between the behavior which we find in KCl and NaCl solutions. In $\frac{1}{2}$ m. or $\frac{5}{8}$ m. NH_4Cl solution the cells are frequently round, without pseudopodia, and the granules are often well preserved. A similar influence is exerted by NH_4NO_3 and $(NH_4)_2SO_4$. It is not improbable that NH_3, formed as a result of hydrolytic dissociation, is in part the cause of the action of the ammonium salts. The ammonium salt solutions inhibit, therefore, directly or indirectly, the changes which may be observed in NaCl solutions. In this case, again, the difference in the behavior between NaCl and NH_4Cl solutions may be demonstrated very clearly if we use combinations of certain solutions; for instance, the combination of 1 c.c. or $\frac{1}{2}$ c.c. of a $\frac{5}{8}$ m. NH_4Cl solution with 2 c.c. of a $\frac{5}{4}$ m. urea solution. In this solution the cells do not form a hyaline network. The cells are round and usually filled with large granules. Sometimes, however, hyaline cells are present, and the nucleus may be pressed to one side. In this solution it is usually easily possible to destroy the cells, which are very soft. It is not difficult to liberate the granules and to produce diffuse masses of granules. The cells in this case are, however, not entirely liquid, but only of a very soft consistency.[1]

[1] Solutions of NH_4Cl have this influence, even if they are used a short time after they have been prepared and if they have been kept in bottles coated by paraffin, so that the action of the alkali of the glass is prevented. It is improbable that secondary changes in the potassium salt solutions are responsible for the action of these salts, the results having been identical with solutions which had been previously kept for different periods. It is, however, intended to make more experiments in this direction next summer.

(To be concluded.)

THE NATURE OF PARATYPHOID FEVER AND ITS CLOSELY ALLIED INFECTIONS.[1]

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It shall be the object of this paper to trace the relations of, and classify in order, typhoid fever, paratyphoid fever, paracolon infection, and meat poisoning by reference to the literature, to which is added some work of the writer, the full details of which will be published in a later paper.

The aberrations of typhoid fever have been long recognized, and an early concrete example of the appreciation of this is offered by the study of Eberth who describes the epidemic at Kloten in which there were 600 cases, the general clinical picture of which corresponded as much to the usual typhoid as to meat poisoning; the origin was undoubtedly the distribution of the meat of a sick calf. There were roseola and enlarged spleen, but it was unlike the fever in its short incubation, mild course, and low mortality (under 1 per cent.). Eberth made an autopsy on each of the two fatal cases and found in the gut and mesenteric glands changes which corresponded to a true typhoid. In reviewing this epidemic he considers the following questions open: Was the Kloten epidemic the usual abdominal typhus? Was it an abortive type or an infectious process probably related? Is there only one true typhoid fever, or is the so-called typhoid fever met with in several forms?

The reasonable doubt of the identity of these atypical cases has become a fact, proven by the same criteria as true typhoid fever, the etiological factor differing from the bacillus of Eberth and Gaffky about as the symptoms approach or disagree with that disease—*i. e.*, the closer the symptoms of the attack the more alike are the biological characters of the organisms apt to be.

The first account of paratyphoid dates at 1896, when Achard and Bensaude isolated from the urine of one case, and pus of an abscess at the sternoclavicular articulation of another, organisms which were practically identical. These cases were clinically typhoid fever with striking symptoms, but sufficiently typical to justify the diagnosis until the micro-organisms were found.

The patients' blood reacted in dilutions of 1:1000; no tests were made with bacillus typhosus with the patients' blood, but antisera of animals immunized against the isolated organisms had no effect upon it, while they agglutinated the corresponding organisms highly, justifying to the reporters the assumption that they were the responsible factors. Again in Paris, Widal, 1897, found a para organism

[1] Read before the Philadelphia Pathological Society, March 9, 1905.

(para is used for all the intermediates of the typhocolon group, pathogenic for man, when a specific type is not needed or given, for the sake of simplicity) in an abscess in a phthisical patient, and considered it the cause of the pus and the slight constitutional symptoms accompanying it.

Gwyn, 1898, and Schottmüller, 1900–01, contributed reports of 7 typhoidal cases from whose blood they obtained paratyphoid organisms. The specificity of their cases was shown by serum reactions, while the bacillus typhosus was not affected by the sera.

Cushing reports finding a bacillus which he calls bacillus "O" in an osteomyelitis of a rib during what was clinically a typhoid relapse. This was also shown to be the causative bacterium by serum tests. In the 5 cases of Kurth, 1901, only 2 gave results to bacteriological search, but the reporter diagnoses the remaining ones by serum tests. The advisability of this will be questioned later.

The reported cases now are approaching a hundred, the diagnosis of some being complete, while that of others is questionable. They were in part sporadic, in part small epidemics, so that a general picture may be drawn to compare with typhoid fever.

Clinical Consideration. No effort is made to describe a new disease on clinical evidence alone, but the variations of this clinical picture can be made comparable to the relation of their causative factors, the paratyphoid bacillus with its subdivisions "A" and "B," and some differences, not absolute or well defined, but reasonably clear, may be said to be presented by the literature at present in each of these types.

The clinical picture of a single case of paratyphoid fever offers nothing to serve as a diagnostic criterion, but many cases collectively may show considerable deviation from the classical picture of abdominal typhoid. The most suggestive fact is the absence of the serum reaction with the bacillus typhosus.

According to the statistics of the Johns Hopkins Hospital 2 per cent. of all cases of typhoid fever present a negative Widal, but only 0.4 per cent. of proven cases give no reaction with the bacillus typhosus.

Here is a discrepancy that may be explained by the inclusions of paratyphoid fever cases in the first figure.

The mortality to date is about 6 per cent., but this will depend upon our opinion of the completeness of data used in making the diagnoses.

The incubation is placed as the same as typhoid fever by Hunermann, who studied the epidemic at Saarbrucken. The stage of invasion is quoted by authors varying from three to eight days, and consists of headache, malaise, sometimes epistaxis, weakness and depression occasionally quite marked. Schottmüller and others especially mention congestion of the conjunctivæ and upper air passages.

A few times mention is made of swellings of the cervical lymph glands and twice of the inguinal. Herpes has been noted and in Longcope's fatal case were present on lips and nose. Neither diarrhœa nor constipation seem to show any supremacy in percentage; they are sometimes accompanied by severe pain in the abdomen.

The onset of the fever is very frequently rapid, and I find three references to an initial chill (A and B, no type) (W and Se., type A) (Sch. 6). In the majority of cases, however, it is the usual step-like advance to the height. After attaining its height the temperature *may* assume the continued type for a few days, but this period is rarely long and is succeeded by marked remissions that do not ascend and descend near the same time of day as in the case with typhoid fever. This may end in an irregular lysis or a crisis with the symptoms usually accompanying such a temperature fall. The duration of the fever is quoted by Clemens as varying from ten to twenty-two days, but by averaging the days mentioned on thirty-one temperature charts the writer obtained an average of 23.3 days.

Brill, 1898, reported 17 cases of continued fever ten to twelve days resembling typhoid fever, but without the Widal reaction. If these be added it will reduce the duration considerably. While this may have been paratyphoid fever it does not seem proper to admit them because they were not proven so to be. Brill's cases showed no premonitory symptoms; a great depression and marked remissions in temperature after a rapid rise over four days.

Roseola are to be found in 80 per cent. of the cases and may be single or in clusters on the abdomen, hands, face, and, according to Brill's cases, very frequently quite marked on the back. According to Hunermann's observations in the epidemic before mentioned, they appear quite regularly about the twenty-first day after the infection. The spots are clear and frequently dark red. Among other skin eruptions are mentioned scarlatinoid, dark macular spots, and petechiæ differing clearly from roseola.

The tongue and pulse are the same in character as seen in typhoid fever, including dicrotism of the latter.

Bronchitis is mentioned in 25 per cent., and more serious pneumonic processes do not seem to be uncommon.

Epistaxis is mentioned in 5 cases, in 1 of which it occurred twice during the invasion period.

Of intestinal symptoms we may find noted all that are present in typhoid fever; vomiting is found occasionally, and in 1 case it was especially obstinate.

Diarrhœa is found at one or another time of the course in 60 per cent., and Brion gives a percentage of 18 for the presence of pea-soup stools. Some cases have during their course both diarrhœa and constipation. At least no material difference can be made out concerning the bowel movements of these disease forms. Pain in the upper part of the abdomen is occasionally mentioned. In some cases of this form of typhoid intestinal symptoms are entirely lacking.

The spleen is enlarged and usually palpable in two-thirds

of the cases; only three times is mention made of its normal size.

Intestinal hemorrhage is encountered nine times, or 10 per cent.; this percentage is made on the whole number of cases regardless of certainty of diagnosis, and when this is taken into consideration with the pathological anatomy it will be difficult to explain. So, too, the pathology will suggest a reason why perforation is not yet mentioned—*i. e.*, the few intestinal lesions noted are quite superficial. The urine is usually febrile, containing albumin, sometimes casts, very many times bacilli, and the diazo reaction may be obtained in about a third of the cases. Four times is mentioned indican in excess and once peptone. Brill's cases gave no indican, acetone, or diacetic acid reaction.

Any degree of mental disturbance from depression to the typhoid state may be present. I do not find any reference to the symptoms of spinal irritation called meningismus.

The leukocyte count, according to Gütig, establishes an analogous picture to typhoid fever, especially with the neutrophiles. There is leukopenia, followed, in the decline, by lymphocytosis (54 per cent.), and a relatively large number of eosinophiles (10 per cent.).

Relapses are mentioned in about the same percentage as typhoid fever, and may follow the initial attack or occur sometime later. They bear the same relation to the main attack as is the case in typhoid fever, while in 1 case (A) two relapses are reported, the second being complicated by a phlebitis in the left thigh.

The limits of the disease, including the relapse, is placed by Johnston at twelve to eighty-four days, but he says "with the exception of the mild cases and in Gwyn's case, the duration of the fever is little indicative of the severity of the attack." The age of the patients varies between seven months and sixty years, the greater majority being between twenty and thirty years. Men are more frequently affected than women, three to one. The largest number of cases have occurred from July to November.

This short account of the clinical course of this type of disease suffices as example of its similarity to enteric fever, but some examples as aberrations are necessary.

The cases of Gwyn and Longcope (fatal) probably best illustrate the similarity to classical and severe typhoid fever, to which they coincided in everything but a serum reaction. In these the bacteriological findings in the blood were the proof of their nature. In contradistinction to these the case of Libman is the most striking. This case assumed the picture of an acute cholecystitis which began suddenly with nausea, vomiting, prostration, followed by distention of the abdomen and pain in the epigastrium and right hypochondrium; last to appear, jaundice. From the gall-bladder by aspiration, and at operation, and the blood, Libman was able to cultivate paratyphoid organisms. The operation revealed a perihepatitis and cholecystitis with an enlarged Riedel lobe.

The objection is raised to the admittance of this case to the class of paratyphoids, that at a limited autopsy fairly typical healed typhoid ulcers were seen, together with some other evidences of typhoid infection, and that the patient's serum reacted in higher dilutions to bacillus typhosus than to the isolated organisms. Nevertheless it can at least be considered here as secondary infection of paratyphoid organisms, since they were undoubtedly the cause of the general septicæmia seen at autopsy. This is the view of the author and is to be emphasized later in contrast to paratyphoid fever.

A quite similar case is one reported by J. H. Pratt, of Boston. This patient had typhoid fever four years before and for two years previous to the present illness complained of pain in the right hypochondrium. At an operation for gallstones the stones showed on culture the bacilli paratyphoid (type "B").

A case reported by G. B. Smith and Walker ("A") shows very clearly how this infection may assume a profound toxæmia. The stage of invasion required seven days; the fastigium presented a continued fever of forty-eight days' duration, followed by a slight return of fever and a distinct relapse three weeks after the main attack. During the forty-eight days of the main attack chills appeared eighteen times; two chills accompanied the slight rise of temperature after the main attack; the relapse was a mild picture of the first, and was accompanied by two chills. The chills were followed by various degrees of sweating. Bacillus paratyphosus ("A") was isolated from the blood. The fever ended very rapidly, twenty-six hours.

Another of Smith's cases was a simple continued fever with two hemorrhages, one amounting to three pints of bright blood and some clots, but no roseola or enlarged spleen (Type "A") was found.

Another of Pratt's cases was a suppurative orchitis (Type "B") and reminds one of the suppurative process mentioned by earlier authors. Allaria in reporting 2 cases in children at two and seven years, lays special stress on a crisis at the thirty-second day in the younger.

Complications. The organisms isolated from the foregoing referred to or described cases have been divided biologically into two groups, but let it be emphasized that it is not necessary to consider these two very widely different organisms. As they vary or resemble the two ends of the typhocolon group, they have been called paratyphoid and paracolon. For the sake of simplicity now let us call all intermediary members of the colon group that are pathogenic for man, paratyphoids. In the laboratory the nomenclature "A" and "B" paratyphoid is given.

The number of cases in which Type "B" has been found outnumbers the cases of Type "A" infection about five to one, according to Pratt. Since his report no material change has taken place in the ratio.

Four "A" cases can be added to 12 described by Pratt;

among the 16 hemorrhage occurred four times, or twenty-five per cent.

We find mention of 1 case each showing as complications thrombosis of the femoral vein, cystitis, bronchitis, and bronchopneumonia (Cushing's osteomyelitis).

Consideration of the complications of Type "B" cases will show a large percentage, especially of the serous membranes (veins, pleura, gall-bladder, peritoneum), which were present in 25 per cent; this figure also represents the proportion of cases showing some involvement of the respiratory tract. Intestinal hemorrhage was present in 5 of 69 cases, 7.2 per cent. of "B" infection. There is mention of 1 case each of embolic softening of the brain, gallstones, nephritis, acute suppurative orchitis, decubitus, furunculosis, and osteomyelitis. Whether the paucity of cases of Type "A" infection is the reason for this low percentage of complications remains for future reports to show. At least one fact is indisputable, that intestinal hemorrhage is more frequent in Type "A" infection. It must be remembered that some cases were afebrile.

The duration of the Type "A" cases is 29.9 days from an average of 13, while that of Type "B" cases is 20.7 days from 16.

Bacteriology. Having recited the clinical phases in a general way it is meet that we should critically examine the etiology of this condition which has been proven biologically different from true typhoid fever. A strict classification of the colon group that is without objections has not been published for many reasons which are not in the province of this paper, but it suffices to say that there are very many different groups within this series, and while the members of these groups are not identical, they agree sufficiently to be classed together. The classical paper of Durham and the description of six strains of paratyphoid organisms obtained by Schottmüller approach the classification of these intermediates from the cultural standpoint, while Buxton combines clinical and bacteriological characters in his orders. The study of this latter supplies a very good working basis since it broaches the subject in this way, thereby serving us as a good introduction to the colon group. This author studied twenty-five cultures of many members of this series, including B. coli communis, B. typhosus (4), B. enteritidis, B. typhi murium, B. cholera suis, B. dysenteriæ (4), B. Hatton (Durham), two of Schottmüller's strains (different types), strains isolated by Gwyn, Cushing, Strong, Johnston (3), Libman, Hewlett, Kurth, and himself. He suggests the following classification for all members of the intermediary groups (except B. dysenteriæ) between the B. coli communis and B. typhosus: 1. Paracolons causing no typhoidal symptoms in man, composed of many different members, but culturally alike. 2. Paratyphoids causing typhoidal symptoms in man, and subdivided into (A) those cultures distinctly unlike the paracolons; (B) those culturally resembling paracolons, but a distinct species. The work of Cushing, Johnston, Schottmüller, Brion, and Kayser in their end results have established nearly identical pictures of the biological reactions of these paratyphoids, and the few individual differences displayed by some of their cultures, and strains described by other authors in their notes of sporadic cases, do not sufficiently disagree to be mentioned. It should be emphasized that these cultures do exhibit individualisms like different strains of any other type. This is notoriously true of the colon bacillus and their allies. The overlapping of biological characteristics is so common as to be misleading at times, and some hope is laid in special serum reactions for the separation of those closely allied. Another point which should be mentioned in the etiological and clinical aspects of these intermediates are the meat-poisoning symptoms caused by some of them, and one group is called the meat poisoners. The paratyphoid "B" are very near biologically to this group, and further on analogies will be made to symptoms and pathology found in cases caused by them. In a personal communication from Dr. Buxton he says: "Between the paratyphoids 'B' and paracolons no sufficiently clear cultural difference can be observed, and I doubt if it is desirable to attempt to classify the paratyphoids 'B' and separate them from the paracolons." In Buxton's grouping the paracolons, group I., consist of B. enteritidis (Gärtner), B. Hatton (Durham), B. cholera suis, B. typhi murium, and one strain isolated by Johnston. The "A" paratyphoids include strains isolated by Gwyn, Cushing, Schottmüller ("A"), Johnston (2), Hewlett, and himself. Among the paratyphoids "B" he places organisms obtained in the cases of Schottmüller ("B"), Kurth, Libman, and possibly Strong, but this last will be found to give some points which seem to exclude it.

For reasons stated above the paracolons and paratyphoids "B" are described together.

Group I. and II. B. They are of typhocolon morphology, usually more actively motile by reasons of flagella peripherally arranged in about the same number as B. typhosus, but by some authors mentioned as longer. Schottmüller describes his members of this class upon gelatin tubes and plates as more luxuriant than B. typhosus and colon, and, after a few days, of porcelain whiteness. He also noted the absence of radial striations seen upon plate colonies of B. typhosus and B. coli communis. Upon Piorkowski's urine gelatin the colonies are round or oval, sometimes yellow, but lacking the long colorless sprouts extending from the oval colonies of B. typhosus on this medium. Upon agar these strains are more luxuriant than the ends of this series. Upon bouillon they produce marked cloudiness. Potato, by Durham and Buxton, receives little respect in separation of these groups, probably because of its varying reaction. However, if there be any characteristic growth of this class, it is in producing a visible brown-tinted covering. After an initial acidity in litmus milk, appearing over

twenty-four hours, members of this group gradually dissolve the casein by production of alkali (average 0.5 per cent.), this alkalinization being permanent, with complete opalescence of the medium in about twenty days. Schottmüller strains gave terminal alkalinity of 1.4 per cent. to 2.8 per cent. Litmus whey will agree with this in behavior to this group. This group will ferment glucose, mannite, fructose, and galactose, but not lactose or saccharose. One per cent. solutions of glucose in sugar-free bouillon and peptone solution are completely fermented in two days, and in yeast broth fermentation ends after twenty-four hours. Neutral red agar is fermented and changed to yellow in twenty-four hours (never over forty-eight hours), which color is permanent.

The other group, A. paratyphoids, resembles those just described in morphology, motility, and in producing a more luxuriant growth in general than B. typhosus. On gelatin it is also without radial furrows and of porcelain whiteness. Upon urine gelatin it appears in very pale round or oval colonies with even margins. Bouillon is moderately clouded (Schottmüller). Potato growth is moist and scarcely visible. Milk is rendered a permanent acid, averaging about 2.2 per cent. at the end of three weeks. Cushing's bacillus is slightly aberrant from this type in the medium. After its initial acidity it returns to a slight alkalinity, 0.3 per cent., and this reaction renders the medium opalescent. One per cent. solution of glucose in sugar-free bouillon require three days for full fermentation, and this process goes on for three days in yeast broth. The other sugars, except as before lactose and saccharose, are fermented. The amount of gas, however, is greater in the paracolons and it requires longer for the subdivision I. to complete fermentation. Neutral red agar is not changed to yellow until forty-eight hours, some of the group losing all the red color, while others retain a little at the surface or at the bottom; this yellow remains for a few days, but at the average of ten days the medium regains its original color. Dr. Buxton in the above-named communication says that a return of color may sometimes be noted among the paracolons, but that it is not complete.

Because of the reaction in milk being supposedly due to some changes in the sugars contained normally (glucose galactose) the previous implantation of B. typhosus to break up this sugar (without gas) renders much clearer the changes produced by these two groups. There is never any coagulation of milk. Under ordinary conditions no indol is produced, but in a peptone solution I find three notes of indol in slight amount with the paracolons and paratyphoids "B."

Very few references are made to the pathogenicity of these organisms, but those mentioned concern the cases when Type "B" was isolated. The organisms isolated by Pratt and Libman when injected into guinea-pigs gave rise to areas of suppuration at the site of inoculation, and post-mortem universal congestion; in one pig a few hemorrhages; and with Libman's organism seropurulent peritonitis resulted in animals injected. Kurth's organisms ("B") produced septicæmia in mice and guinea-pigs. I find no detailed references of value with injections of Type "A," and while these cases may be too few, yet they are supported by clinical facts. The symptoms of septicæmia in Libman's case (cholecystitis, etc.), the suppurative orchitis reported in one and saphenous phlebitis in another of Pratt's cases, and the pictures of septicæmia of Allen's cases are all examples of Type "B" infection. Type "A" can produce pus as shown by Cushing's growth from an osteomyelitis. But the point is made that from the standpoint of pathogenicity, as well as in biological relations, Type "B" stands near the group of meat poisoners. The picture of septicæmia and toxæmia in meat poisoning is well known both in man and in experimental animals; the latter taking the infection by mouth as well as by injection with the same results. Pus at the site of injection is common. The complications of meat poisoning are the same as those detailed for Type "B," but of greater severity.

These organisms have been obtained, some at post-mortem, but most of them during life, in the blood, urine, feces, rose spots, spleen, by puncture, vagina, and pus of abscesses. They appear in some cases to be in large numbers, for Gwyn, Brion, and Kayser, instead of using large quantities of bouillon requisite for the isolation of the B. typhosus, simply spread a few cubic centimetres of blood over solidified agar.

Serum Tests. For the purpose of separating this paratyphoid fever and allied infections from typhoid fever, many serum reactions were undertaken, as was to be expected, coming, as these new descriptions did, so soon after the introduction of serum diagnosis in disease. The first results seem to be more conclusive than the later ones, and it is questionable whether the refinements will assist much, since the first few observations proved fairly conclusively that here we have to deal with an infectious disease close to typhoid, especially in etiological consideration, and therefore probably subject to the same disseminating factors.

As was first thought, the high percentage of clinical typhoids with negative serum agglutinations was probably due to the inclusions of some para infections. When the first results were obtained it was thought that the agglutination of paratyphoid organisms with a patient's serum that showed no such reaction with the bacillus of Eberth was a nearly or quite pathognomonic point for the existence of para fever. This was used as a substantial support to the acceptance by Schottmüller, and those following him, of the specificity of their isolated germs. Later some interaction of members of the intermediary groups with B. typhosus led several investigators to work out these relations.

To return to some of the old work for a moment, we find the Achard and Bensaude's organisms were clumped by the patients' serum and slightly by antityphoid serum,

while the patients' serum reacted with three strains of B. psittacosis (Nocard), giving rise to the suspicion in the observers' minds that they were dealing with an organism like this last.

Widal's patients' serum agglutinated the isolated organism, but did not affect other members of the colon group. Schottmüller's experiments showed that his Type "A" (two strains) were not clumped or only slightly affected by the serum of Type "B," while this group were well clumped by their own patients' sera, and besides this interagglutinated. However, the serum of one of the patients belonging to each group agglutinated all organisms; Type "A" serum acting in the same dilution for all, while Type "B" serum was more potent for Type "B" strains.

Cushing obtained a highly potent antiserum for his strain (1:8000) which had no effect on Gwyn's strain, B. typhosus or colon bacilli. This antiserum did interagglutinate with B. cholera suis, and an antiserum of this latter germ reacted with Cushing's organism, but with no other member of the series.

Durham demonstrated this absence of interaction of Gwyn and Cushing in a manner reversing that mentioned above, but says he can hardly distinguish these two organisms culturally.

Other observers, Kurth ("B"), de Feyfer, and Kayser ("A"), Wells and Scott ("A"), and others mention that no considerable agglutination took place with their antipara sera and the bacillus of Eberth, while they reacted in high dilutions with their own and analogous strains. Here also the extensive work of Buxton comes into consideration. He immunized animals against all the strains mentioned before in this paper and tried each of these antisera with every organism. Unfortunately the anti-Gwyn rabbits died before its serum was tried with all the strains. The trials made, however, are sufficient to be accepted when taken into account with others of this group.

His dilutions and time limits were 1:400 and four hours respectively. In so far as the members of his paratyphoid "A" group are concerned, they mutually interacted completely, but not with any other of the colon series, and he considers these results ample proof that these strains are a true species and not merely a group. He found, contrary to the results of Cushing and Durham, that strains "Gwyn" and "Cushing's 'O'" did interact, and is at a loss to explain the failure of these observers. Let it be remembered here that B. "O." varies a little from Type "A," of which Gwyn is a good representative.

Type "B" was not uniform in its reactions, but he makes plain that those organisms which do not cause typhoidal symptoms in man and the typhoid bacillus do not interagglutinate with these "A" and "B" paratyphoids.

With regard to this last statement much further discussion will be necessary, for it has not been found absolutely true. Buxton immunized an animal against both types and found that the serum may have a clumping effect on both types without losing its effects on the one first used for injections. Still the foregoing facts will not answer the questions which arise to our minds: Will the serum of a true typhoid fever patient agglutinate the paratyphoid organism? And will, on the other hand, the serum of a paratyphoid fever patient clump the B. typhosus?

With reference to the first, the writer offers the results of the experiments mentioned before at the University Hospital, where the serum of all cases coming for Widal examinations are routinely tried with "A" paratyphoid organisms. With the exception of 12 cases among 94 the results were negative, 4 of which were proven to be true typhoid by blood culture. In 3 were the dilution limits for "A" paratyphoid the same as for B. typhosus, 1:500; in 2 were they 1:250 and exceeded by the limits for B. typhosus. Two cases giving reactions with "A" paratyphoids in dilution 1:500 and 1:250 were proven typhoid fever, the remaining 2 only reacting in 1:50. The agglutination curve for the highest reactions is given here (Chart I.) outlined

Chart I.

for B. typhosus, paratyphoid "A" and "B," and bacillus of Gärtner. It will be noticed that the curve of the "A" paratyphoids throughout the attack, and even more so in the relapse, exceeded that of the typhoid bacillus. This would seem to indicate that the blood culture missed the "A" paratyphoid. This question came up during the illness, but as the patient was a private one in the hospital, a further study was not permitted. The result of the blood culture was considered final, but if we assume that the isolated bacterium was the only cause of the attack an explanation of these curves is not easy. Some light on a possible explanation will be given later.

This contributes to work by Jürgens, von Drigalski, and Conradi who worked with Type "B" and found that unlike the foregoing the reaction of the twenty-two patients in a typhoid epidemic at Trier, with one exception, reacted quite strongly with this "B" type. They found that this reaction usually appeared about the same time as the antityphoid, but sometimes it was several days later, once eighteen days later. However, five times the reaction to the paratyphoid appeared earlier than that to the typhoid bacillus. Their first case died when the reaction to the former was higher than that to the latter, yet at autopsy there were found only the bacillus of Eberth. Usually this organism was agglutinated in higher dilutions than the other, but in four cases was the reaction appreciably higher at one time or another; especially was this the case at the beginning and end of the attack. The agglutination dilution curves did not coincide exactly throughout, but in general rise and fall they followed the same course (Chart II.). In those cases

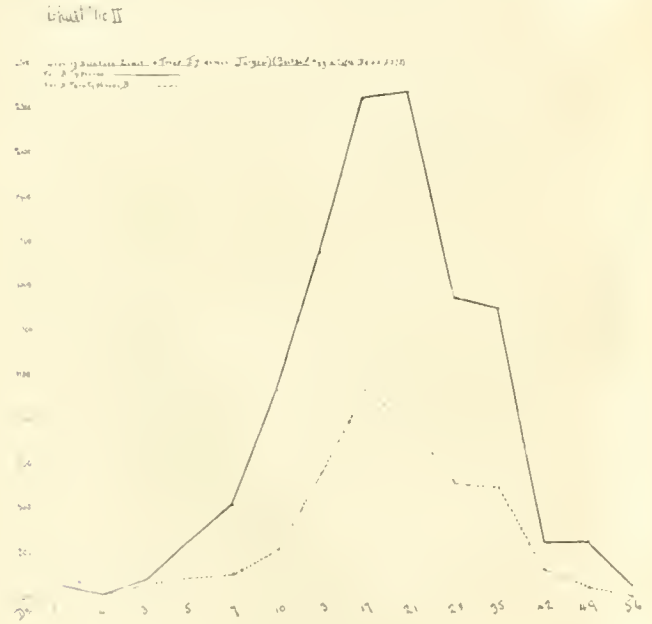

Chart II.

where the absolute limit of the dilution was considerably above the B. typhosus, for the paratyphosus "B," nothing but the first mentioned was found on bacteriological search.

With this evidence may be coupled the studies of Bruns and Kayser, who carried out a large series of experiments with various colon group antisera.

When using a very highly potent antityphoid serum (1:50,000) they were able to obtain with Schottmüller's two types strains of Kayser ("A") and Kurth ("B") positive reactions in dilutions of 1:500, the same dilution giving similar results with some of the meat poisoners—*i. e.*, corresponding to Buxton's paracolons, and with the strains Gaustad and Friedebergensis particularly the dilution limits reached 1:1000.

When they used sera of potencies 1:5000 and 1:1000 respectively the difference is striking, for with no organisms but B. Friedebergensis, which reacted feebly at 1:100 with the more potent serum, did they obtain a positive diagnostic reaction. On the other hand, the use of a Type "A" antiserum showed clearly the relationships in all dilutions between organisms decided culturally to belong to this species. Two Type "B" antisera (Schottmüller "B," 2500 potency; Kurth "B," 2500 potency) clearly outlined their effects to their own group, but at the same time agglutinating one meat poisoner, which is closely related biologically, and certainly affected several strains of B. typhosus in dilution of 1:100. A B. coli antiserum agglutinated some of the paracolons indistinctly and gave a questionable reaction with one typhoid strain and one paratyphoid "B."

Rolly tested the serum of 40 true typhoids with types "A" and "B," B. enteritidis (Gärtner), and the B. typhosus. Seventy per cent. of these sera clumped the paratyphoid bacilli regardless of type, and half that number gave reactions in higher dilutions than the B. typhosus did. Only 16 of these 40 cases were examined between the first and fourth week, the remainder being tried during the convalescence; 19 reacted to the Type "A," of which 5 sera gave no reaction to Type "B." Nine of this 19 reacted to Type "A" in higher dilutions than they did to the B. typhosus. To Type "B" the typhoid serum reacted twenty-two times, and 8 of this number did not clump Type "A." Seven of this 22 gave higher limits for Type "B" than for the typhoid bacillus. A noticeable point that the author does not mention is that of the 16 cases examined during the fastigium only 3 gave a more positive reaction to paratyphoids than to typhoid bacillus. Notwithstanding these results, which are contrary to those just described, the work of Rolly concerns too few cases at unfavorable times and only one test in each case, thereby giving no basis for causes or conclusions. He obtained positive agglutinations of Type "A" in 48 per cent. of his typhoids, while the writer observed this in only 12 per cent.. One of Rolly's results is worth mention, and that is in these sera the B. enteritidis (Gärtner) and Type "B" were not clumped at or near the same dilutions.

Having proven fairly conclusively that typhoid serum may react to the B. paratyphosus, let us consider the second question—*i. e.*, whether the reverse is true. If we look over the literature of cases we find that some were absolutely negative to B. typhosus, while others reacted in low dilutions; and the lowest limits and for a positive Widal, so far reported, have been in cases of Type "A" infection. In examining the Saarbrücken epidemic, which was of the "B" type, marked agglutination of B. typhosus will be found. Thirty of the 38 cases showed a positive "B" paratyphosus reaction in dilution of 1:100 or higher, while of this number 26 gave an agglutination of the Eberth bacillus at the same time. The 4 in which the reaction was absent were

examined early in the disease in 2 and quite late in the others, so that the reaction to the B. typhosus may not have appeared or had already disappeared. In nearly all of these cases were the paratyphoid bacilli proven in the stools.

Upon consideration of the foregoing conflicting evidence the following questions naturally present themselves for decision:

1. What relation does a negative Widal bear to the existence of paratyphoid fever?

2. What is the relation of Types "A" and "B" of paratyphoid bacillus to the B. typhosus and members of the intermediary groups?

3. How shall we decide upon the existence of a mixed infection when a double agglutination occurs?

4. What shall be our diagnostic criteria and what shall be our dilution limits when there is coincident agglutination of two or more organisms?

In reference to the first question, may it be called to mind that an absence of a Widal reaction is not a sure proof that the patient is not inhabited by the typhoid bacillus. A positive reaction may be wanting in cases which are clinically and indubitably typhoid and also where B. typhosus has been found in the stools without subjective signs of an attack. Given a negative result in two hours after combination of a patient's serum with two or more strains of B. typhosus in 1:100, when the case closely resembles enteric, one would be inclined to search for a positive parareaction, but we must not forget to take into consideration the days of disease. Early in the disease, for example, probably the entire first week, may no positive Widal be obtained. Again, after the disappearance of the fever the same result is sometimes seen. The curve, which is made by the limit of agglutination, is by no means regular.

The relation of Types "A" and "B" paratyphoids to B. typhosus seems to differ when considered from biological and serum agglutinative standpoints. If one review the cultural characters of the former group it will be found quite near to the B. typhosus, and, as mentioned several times, Type "B" approaches the meat poisoners of the B. enteritidis type. According to Schottmüller Type "A" resembles organisms of the type paracolon of Buxton—*i. e.*, B. Breslaviensis and B. Friedebergensis, which are meat poisoners, the former being classified by Van Ermengen as quite near to B. Hatton (Durham). Schottmüller found no organism reported which he considered identical with Type "B."

Notwithstanding Schottmüller's dictum, antisera of Type "A," according to the extensive work of Bruns and Kayser, had no agglutinative effect upon B. Morseiliensis, B. Friedebergensis, B. morbificans bovis, or B. Breslaviensis. The last named, however, was given a place near Type "B" because it reacted with antisera of this type nearly as strongly as the homologous bacillus. Antisera of high potency produced by injections of B. typhosus, as before detailed, clumped both "A" and "B" types to the same limits, while those of lower potencies had no effect upon these groups. The antisera of Types "A" and "B" had no effect upon the heterologous strains and were clearly special for their own groups. The B. typhosus was clumped by antibacillus "B" sera up to 1:100, which would seem to indicate a close relationship between these two organisms.

The results of these experiments agree in part with Buxton's work, except that he found no interaction between Type "B," B. typhosus organisms, and sera.

All these facts remind one of Durham's statement that organisms culturally near one another may show no tendency to interagglutinate, while types easily differentiable biologically may show this mutual interaction. By this is explained the failure of the writer to obtain reactions with Type "A" with the typhoid patients at the University Hospital, and raises the question why the twelve exceptions occurred. Durham's dictum also is admissible in connection with Jürgen's work with paratyphoids "B" in the Trier epidemic.

The presence of the bacillus of Eberth in some healthy intestinal tracts is not doubted; therefore, may it not be accompanied by some closely related organism? Conradi was able to isolate B. of Eberth and a paratyphoid from a true typhoid stool and a normal one. They were of the "A" type. This is the first question which presents itself, especially when we consider the coincident clumping of this organism and another. This possibility is not doubted, and that they might both gain entrance to the blood stream is not questioned. It has been suggested that they produce some common agglutinating body and thereby a twofold reaction occurs. It has been shown with regard to the microorganisms in question that it is not necessary that two types of germs be present; that one may produce an agglutinating body to which the other is susceptible. It would be supposed, because of bacteriological similarity of the Type "A" paratyphoids and the B. typhosus, that they would give rise to some such mutually reactive product. Schottmüller is the only observer to note the interagglutination of these two types, while experiments on immunized animals do not establish it. The explanation of these curious phenomena *may* be found in Durham's hypothesis. He supposes an agglutinin to be a complex body, while the bacillary components capable of giving rise to this agglutinin are equally complex. The agglutinin he represents with capitals, and the bacillary components with the corresponding small letters. Since B. typhosus and B. enteritidis (Gärtner) are known to interagglutinate, and B. Hatton will not react with either, he takes them for examples. He supposes B. typhosus to be composed of a+b+c+d+e and its corresponding agglutinin to be A+B+C+D+E. B. enteritidis agglutinins he represents as C+D+E+F+G+H, B. Hatton as E+F+G+H+J+K, with the small letters like the capitals representing their bacillary components.

When homologous bacilli and clumping body are added together in like amount the maximum results are obtained. But suppose the B. enteritidis be added to B. typhosus antiserum (e+f+g+h+c+d)+(A+B+C+D+E) the reaction will be in proportion as the common elements C, D, and E can combine. If to the bacillary components of B. Hatton are added the agglutinating bodies of B. typhosus the strength of the latter will have to be relatively stronger to obtain an appreciable reaction because they contain only the common element *e*. Durham further supposes that these various constituents are not present in the same amounts in any two cultures or any two members of a species, but considers that they may be multiplied by various factors. Now, if the common constituents of two organisms which are tried together were only in low proportion, so much the greater would have to be the amount of the serum in order to affect their common members among the bacillary components of the other organism.

This may be accepted as partially explaining these crossed reactions. The real question of positive establishment of a mixed infection can only be reached by proving a double bactericidal property of the serum in question and whether this later may or may not be saturated by one or the other organism. These are called Pfeiffer's and Castellani's tests, respectively.

Of course a double bacterological result to cultures from blood or other site is positive if there be at the same time a double reaction to the organisms isolated or to members of their type. A body cannot be said to be infected with an organism unless it has reacted to the same, which reaction may be demonstrated by subjective symptoms or objective phenomena—*i. e.*, agglutination or bactericidal influence. If we obtain from a typhoid case a repeatedly positive agglutination of Type "A" paratyphoid and no reaction at all to B. typhosus we may consider it a Type "A" infection, but this may not be taken unquestioned with Type "B." Even if Type "A" give a positive result and B. typhosus a negative one, still will the bactericidal influence of the serum render all questions answered.

With Type "B," however, the positive character of the infection must be determined by an unquestionable agglutination of this type throughout the attack with no result when B. typhosus is used, if we desire to absolutely justify its etiology. But this cannot be done, since Type "B" infection will clump B. typhosus; so that we must take refuge in isolation of the causative bacillus from the blood, feces, or other means. If this gives a Type "B" culture and one still raises the question of mixed infection, certain graded dilutions of the patient's blood, to which is added established amounts of Type "B" culture in the first experiments and B. typhosus in a second set, may be injected into guinea-pigs' peritoneal cavities. The organisms rendered harmless by the least amount of serum may be considered as the type of germ giving rise to the attack in question. Should these results be conflicting as to leave doubt, the test of Castellani is left to us. This depends upon the fact that the agglutinating property or body of a serum may be exhausted for the both organisms giving the positive results, when it is saturated with the etiological bacterium, while saturation by the co-agglutinated organism will not decrease the limit of agglutination for the causative factor.

Bruns and Kayser say that a quick diagnostic test may be made by 1:75 dilution using a twelve-hour bouillon culture of the organism, "but it is desirable to obtain the limit of dilution possible to give a reaction." Be it emphasized again, it depends upon the organism used and that the reaction must be repeatedly positive in higher dilutions than that obtained by any other organism, to which should be added, if possible, the proof of bacteriological culture, saturation, or bactericidal phenomena. According to many observers, agglutination in disease is only an elevated value of the normal agglutinating bodies of the blood, and if a sufficient study of low dilutions were made on all bacterial diseases it would probably show an agglutination on higher dilutions for all organisms, pathogenic for man, than is present normally.

If this enhanced value of the normal agglutinin in disease is accepted as explaining all co-agglutinations, why then should not so closely related an organism to the B. typhosus as the Type "A" be affected by true antityphoid sera? Apparently we must search further for an explanation, and the suggestion of Meltzer, Durham, and others, that some constituent of a specific agglutinin is also produced by another organism, gains in weight.

With reference to the relation of this paratyphoid fever in man to meat poisoning in man, the work of Bruns and Kayser before mentioned shows an agglutination of the causative bacteria of these diseases about the same as is the case with typhoid bacillus. Especially are the meat poisoners B. Gaustad and B. Breslaviensis related to the Type "B" paratyphoids, if we were to accept serum reaction as proof. Probably the same criteria suggested for the diagnosis of typhoid-like cases in man may serve as means for differential diagnosis, should there be any question of the relations of acute septicæmic symptoms to this "B." type or its closely related forms.

Pathology. The point the writer wishes to make with reference to this subject, coupled with the clinical phases of the reported cases, is that differences can be noted in Types "A" and "B" infections, even though the lines may be ill-defined.

After reviewing the known pathology of this condition, Kieth comes to the conclusion that for the present this form of disease must be considered as a general acute infectious process for which a certain determined local lesion does not exist.

According to observers of autopsies on para infections no close similarity exists in the pathological picture to that

of typhoid. So rises the question whether some cases that have been classed as typhoid without intestinal lesions have not been of this type. This question may, I think, be answerable in the affirmative if one refers to those cases of paratyphoid "B" where a positive agglutination of the B. typhosus was observed. But of the pathology of those instances where there was more than a suspicion of the existence of a para infection, we have only a few cases. Wells and Scott have collected four autopsies of such cases and add one of their own. Of these cases four were of the "B" type, one of "A" type. I can do no better than quote verbatim the summary of their investigations: "There is little characterizing this type of infection or differentiating it from other septicæmias anatomically however much it may differ clinically. The most constant change is the enlargement of the spleen, which was present in all five cases. In most respects this enlargement seems to be the same as that of typhoid or ordinary septicæmia, and in our case the microscopic findings are similar. The loading of the splenic endothelial cells with pigment and erythrocytes is evidently the results of the hæmolysis of the disease. The intestinal lesions are, however, quite variable. Because of the occasional occurrence of intestinal hemorrhage it had at first been thought that intestinal ulcerations probably were present, although the first cases autopsied, those of Strong and Longcope, showed the intestines to be quite unaffected. In the last cases, however, there have been numerous ulcers, although entirely different from those of typhoid. In our case, in which the hemorrhages were a prominent feature of the attack, the largest amount of ulceration of any of the five was found. The reporters of the cases in which the ulcerations were described, agreed in likening them to those of dysentery rather than to those of typhoid. In all cases there was also a practical absence of any alteration of Peyer's patches or of the solitary follicles. Likewise the mesenteric glands were almost unaltered. Strong alone reports swelling of the glands, which were not microscopically examined. Lutksch found one enlarged gland with endothelial proliferation. In the other three there were no gross changes in them and in none does there seem to have been any generalized glandular hyperplasia. In Longcope's case and in ours (Wells and Scott) there were typical focal necroses in the liver differing from those in typhoid fever in not containing endothelial cells. Beyond these changes there seem to be none of significance."

If to this is added a description of the ulcers found by Wells and Scott the difference to those of typhoid is not difficult to see. Those described by these observers were seated in the lower ileum, quite superficially, rarely going through the muscular wall, indeed many having the submucosa as a base. They were sharply outlined, frequently coalescing and lacking any reactive inflammatory process in their margins or beyond them. They were, however, slightly undermined. There was *no* congestion of the intestinal wall in this case. This is the representative case of Type "A" infection.

Type "B" pathology may be represented by Longcope's case, which was a typical clinical case of typhoid fever, yet upon autopsy there were found only enlarged solitary follicles, soft spleen with a few hemorrhages, and cloudy swelling of the liver. There were ascaris lumbricoides in the intestine and the mesenteric glands were free from lesions. From various organs the same bacillus was isolated as was obtained from the blood ante-mortem.

Besides this case may be taken the one reported by Strong. From the spleen of a typhoidal case this observer cultured a bacillus conforming to Buxton's "B" type, which was pathogenic for mice. The mesenteric lymphatics were swollen, and some along the small intestine were hemorrhagic. The only pathological offerings of the intestinal tract was a catarrh and a few hemorrhges. The lymphatic apparatus of the bowel was not affected.

Sion and Negel's case may be mentioned in which, besides an embolic softening of the brain, bronchitis, and pneumonia, there was a dysenteric inflammation of the lower ileum; no ulceration, but a swollen, injected intestinal wall covered by necrotic detritus, while the lymphatic structures were not affected.

Libman's fatal case was not accepted by Wells and Scott for the reason already stated—*i. e.*, a positive Widal, thereby sharing the reporter's opinion that it was a mixed infection. Also at autopsy typical healed typhoid ulcers were found, which strengthened this opinion. Nevertheless, the B. paratyphosus, Type "B," was isolated; and because it serves to represent a case of Type "B" infection and because by styling this case a mixed infection the author must have accredited to the isolated germ some etiological significance, it is included here. It is the opinion of the writer that this organism was the cause of the attack, because the Widal was positive after several negative results had been obtained while the organisms were clumped, which were obtained shortly after their isolation and before the appearance of the Widal, even if only in a low dilution. The correctness of this opinion cannot positively be asserted. This attack was quite acute and assumed the picture of an acute cholecystitis with symptoms of septicæmia. An autopsy, which was limited by the patient's family, showed the typhoid scars as mentioned above, together with evidences of congestion of all the organs, especially the liver and spleen. It appears here that the attack and pathological results were more like a septicæmia than a true typhoid fever. The existence of the healed ulcers of typhoid fever (limited autopsy) cannot be satisfactorily explained.

Perhaps the one case of Type "A" autopsy is not enough upon which to base arguments; still some deductions may seem justifiable when this case is taken into consideration clinically.

As noted above, the greatest amount of ulceration of any

autopsy was found in this case of Wells and Scott, which gave a clinical course of typhoid fever including intestinal hemorrhages. In these two respects do they agree. The duration of Type "A" infections from an average of 13 cases is 25.9 days; while the duration of proven Type "B" cases from an average of 16 is 20.7 days. The former figures are surely nearer the average length of typhoid fever than the latter. The Type "B" epidemic at Saarbrücken would rather tend to shorten this time. On the other hand, Type "B" infections give more strikingly the picture of a septicæmia, and in these the part taken by the intestine is usually a general catarrhal or hemorrhagic enteritidis without so great tendency to localize itself into ulceration. The case of Longcope may be cited as one clinically approaching the "A" variety, but cases of meat poisoning have repeatedly given a clinical picture very like this case. Most of the attacks produced by the meat poisoners are of short duration, but this is by no means absolute. Sometimes, indeed, the convalescence is slow in appearing and very tardy in disappearing. The pathological anatomy of meat poisoning may vary from a slight catarrh to a virulent hemorrhagic inflammation of the entire gastrointestinal tract. In our Type "A" case, as in typhoid, the changes in the mucous membrane of the gut were limited to the region of the ileum, while in the other cases they were not determined in location. Lutksch noted changes in the stomach and colon, Longcope in the colon, Sion and Negel in the ileum, while Strong's notes seem to indicate that the lesions were scattered.

Objection may be made to this likening these "B" cases to meat poisoning, because in some autopsies on the latter Peyer's patches have been swollen. In answer to this it may be said that those cases of meat poisoning which came to autopsy early enough to have these agminated glands enlarged, show also lymphatics involved having no connection with the intestinal tract, while I find no references to peculiar ulceration of Peyer's glands. Vomiting, which is common in meat poisoning, is noted in some "B" cases, but none of the "A" type.

To these arguments for the more septicæmic nature of Type "B" than may be ascribed to Type "A," let us examine the complications of the former. The pyogenic properties have been well demonstrated and metastatic processes noted. The involvement of the endothelial membranes has been mentioned. All of these results may occur in meat poisoning more frequently than typhoid fever. The greater number of complications in this type speaks for a more acute septicæmic process. The percentage of hemorrhages per rectum is greater in Type "A," as would be expected, if the opinion that this form is nearer to enteric fever than the other is considered admissible. Hemorrhages, for reasons cited in the pathological details, may *also* be expected in the "B" types.

A case may be quoted in objection to these views. It is Smith's prolonged case, in which there were so many chills and clinical evidence of toxæmia, while Type "A" organisms were isolated. Some cases of typhoid fever may evidence toxæmic symptoms, and while such a course as described by Smith is uncommon in true typhoid, could there not have been a mixed infection with some of the kind of bacterium? Even if this contingency is not allowed—and we admit that clinically this oversteps the line of distinction defended here—it does not materially alter the general classification. I wish to impress upon my readers that I make no sharp distinction between typhoid fever, paratyphoid fever ("A" and "B") infections, but have attempted to point out that the relationships existing between the clinical symptoms and pathological pictures are very similar to the positions in which we place the etiological factor—*i. e.*, the organisms. If we begin at the end of the colon series where the bacillus of Eberth and Gaffky is placed and proceed toward the colon type, we meet in order the Type "A" first, the Type "B" next, which is closely followed by the meat-poisoning groups, and such may be described the order of the clinicopathological demonstrations of these bacteria. This accords with Trautman's views that clinically we may consider the meat-poisoning symptoms in general as hyperacute, para cases on the whole as acute, and those of true typhoidal nature as more subacute.

A point which must receive some consideration is the favorable prognosis given by some authors, notably Schottmüller and Kurth. The cases reported by these two observers probably were true para infections, but when we consider some of the cases, especially of the "B" type, that were diagnosed by serum tests which are notably liable to error, we must have care as to our mortality percentage. Of the "A" type there is surely one autopsy of 16 cases here referred to, while of the *diagnosed* "B" infections 5 deaths occurred. The latter are so much the more numerous, and at the same time rather untrustworthy, that the actual mortality is difficult to obtain. In the Saarbrücken epidemic no fatalities happened among 38 cases ("B" type), which would speak for a favorable prognosis. At any rate, the only thing that seems justifiable to say is that the statistics obtained do not differ greatly from those of typhoid fever. Certainly 90-odd cases of this may be picked indiscriminately from the same various places in which para cases have been reported and not show more than 6 deaths. Of *proven* paratyphoid infections the mortality is *about* 10 per cent. Until we have more positive diagnoses we can lay no stress upon a more favorable prognosis.

As is the case when any differentiation in form of a general idea of a disease is presented, so is there a discussion regarding the name of this new variation of the typhoid etiology. The name of this presentation is best described by the introductory remarks, and justifiably may be considered as a type of typhoid fever varying in different ways from its classical picture and sufficiently in etiology to deserve special description. But all the cases to which have

been given this name are not of the enteric form, to wit: Libman's cholecystitis, Pratt's gallstone case and suppurative orchitis case, Smith's prolonged toxæmic case, Widal's case of an abscess in a phthisical patient with slight constitutional symptoms, while the pictures of Allen's cases vary less from typhoid than the foregoing. There are others where noticeable differences were mentioned and the majority in percentage are of Type "B" infection, so that we may say "paratyphoid" is with greater propriety applied to Type "A". To object to this may be cited the very typhoid-like case of Longcope. In answer may be said that acute tuberculosis assumes this form, while malaria has been known to be confused. Then again we are not drawing any sharp lines and speaking more in generalisms. Meltzer defends the name paratyphoid for the whole class, because it suggests the clinical phase of the attack and the organisms are nearer the B. typhosus than the B. coli. "Bacillus paracolon" and "paracolon" fever he thinks are not sufficiently specific. Libman objects to "paracolon" because it relates the attack and the bacterium too closely to the B. coli communis, while "paratyphoid," according to his opinion, should be used for organisms identical to the bacillus of Eberth, but not interagglutinative with it. He concludes the choice lies between these two until we have differentiated the micro-organisms more clearly.

If it be necessary to name these forms some reference will have to be made to the etiology and pathology mentioned in part of the foregoing remarks. So far as attempting to entirely destroy the present conception of typhoid fever and its various abortive or atypical forms, no good can be hoped for unless at some early time we find specific therapy. If it be considered advisable to apply names to the cases which display all of the characters of the infection and the etiology detailed to the extent of our present knowledge obtained from the literature of cases and of experiments, the following nomenclature is offered for discussion.

Let us consider the true typhoid fever, no matter what its manifestations, but in which the etiological role of the B. typhosus is undoubted, as typhoid or enteric fever or typhus abdominalis. Its next relation whose etiology is the "A" type let us call the paratyphus infectiosa and the organism B. paratyphosus infectiosa or B. paratyphosus "A." Because of the greater septicæmic character of the "B" cases, the name of paracolon septicæmia is suggested, and an analogous name for the bacillus. The cases partaking of both characters are thereby considered as transitional types varying in like manner as do the various members of the groups.

A consideration of all the facts in this general review of the position of paratyphoid fever seems to offer the following conclusions:

1. Paratyphoid fever differs from typhoid fever in (*a*) a shorter invasion stage and rise of temperature; (*b*) shorter or absent period of continued fever; and (*c*) marked diurnal remissions of temperature, much deeper than enteric and without periodicity. An absence of the Widal is suggestive, if it persist in reasonably high dilutions.

2. The duration is on the whole shorter than typhoid, and the cases where Type "B" was adjudged the etiological role this fact is more striking than in the Type "A" cases.

3. The general findings of the Type "A" cases are nearer to typhoid than Type "B," the latter presenting a picture more like septicæmia.

4. The complications of Type "B" infections are more numerous, more purulent, and the course is more fulminating in these cases.

5. The causal germs belong to the intermediates of the typhocolon series, the Type "A" being nearer to the bacillus of Eberth and Gaffky, while Type "B" approaches the meat-poisoning group.

6. The clinical evidences of the respective organisms just named agree with their general properties and relations to infections in this order, ranging from the subacute typhoid to the hyperacute meat poisoning.

7. Antityphoid serum will clump the paratyphoid "B" at the same time as the B. typhosus, sometimes even in higher dilutions; so that a positive reaction of a patient's serum to both B. typhosus and paratyphosus "B," even if the latter be in higher dilutions, will not permit a diagnosis. On the other hand, only twelve times in 94 cases of typhoid fever did the serum react with the Type "A" paratyphoid; so that a positive reaction with Type "A" and not with the bacillus of Eberth may be taken as nearly a proof of the existence of an "A" paratyphoid infection.

8. That there must be some other factor responsible for coagglutinations than an increased value of the agglutinins normally present in the blood seems probable.

9. That the best proof of the existence of a para infection is the isolation of the bacterium, the saturation test, and, last, the bactericidal action.

Bibliography.

Brill, N. E. New York Medical Journal, February 15, 1898.

Schottmuller. Deutsche med. Woch., 1900, p. 501; Zeitschrift fur Hygiene u. Infk., 1901, Bd. xxxvi.; Münch. med. Woch., 1902, No. 38.

Gwyn. Johns Hopkins Hospital Bulletin, 1898, p. 54.

Kurth. Deutsche med. Woch., 1901, p. 501.

Cushing. Johns Hopkins Medical Bulletin, 1900, p. 156.

Widal. La semaine méd., August, 1897.

Achard and Bensaude. Bull. et mém. Soc. méd. des hôp. de Paris, November, 1896.

Durham. Journal of Experimental Medicine, vol. v. p. 353.

Gütig. Präger med. Woch., 1903, Bd. xviii.

Allaria. Riforma Medica, 1903, No. 49.

Jürgens. Zeitschrift f. klin. Med., Bd. lii. p. 40.

Jürgens and Bruns and Kayser. Zeit. f. Hygiene u Infk., 1903, Bd. xliii.; Deutsche med. Woch., 1904, No. 34.

Trautman. Zeit. f. Hygiene u. Infk., Bd. xlv. and xlvi.

Flatau. Münch. med. Woch., Bd. li., No. 26

Evans. Medical News, September 3, 1904; New Orleans Medical and Surgical Journal, November, 1901.

Hunermann. Zeit. f. Hygiene u. Infk., Bd. xl. p. 522.

Neufeld and Van Ermenghen. Handb. f. path. Mikroorg., pp. 279 and 652.
Zupnik and Posner. Prager med. Woch., 1903, No. 18.
Pratt Boston Medical and Surgical Journal, February 5, 1903.
Erne. Münch. med. Woch., Bd. li., No. 34.
De Feyfer and Kayser. Münch. med. Woch., 1902, Bd. xlix. pp. 1692 and 1752.
Sion and Negel. Zentralblatt f. Bact., Bd. xxxii. pp. 482-581.
Kayser, H. Deutsche med Woch., 1904, Bd. xxx., No. 49.
Lutksch. Zentralblatt f. Bact., Bd. xxxiv., No. 2.
Pascual. Brooklyn Medical Journal, April, 1904.
Conradi. Deutsche med. Woch., Bd. xxx., No. 32.
Coleman and Buxton. American Journal of the Medical Sciences, June, 1902.
Johnston. American Journal of the Medical Sciences, August, 1902.
Hewlet. Ibid.
Longcope. Ibid.
Meltzer. New York Medical Journal, January, 25 1902.
Allen. American Journal of the Medical Sciences, January, 1903.
Kayser. Deutsche med. Woch., Bd. xxix., No. 17.
Schmidt, R. Münch. med. Woch., Bd. xl., No. 49.
Ascoli. Zeit. f. klin. Med., Bd. xlvii.
Smith, G. B. Journal of the American Medical Association, vol. xli. p. 1470.
Walker. Ibid., p. 1472.
Buxton. Journal of Medical Research, 1902, No. 8.
Libman. Ibid.
Strong. Johns Hopkins Hospital Bulletin, May, 1902.
Clemens. Deutsche med. Woch., Bd. xxx., Nos. 8 and 9.
Rolly. Münch. med. Woch., 1905, No. 3.
Wells and Scott. Journal of Infectious Diseases, January, 1904.

BOOK REVIEWS.

EPILEPSY AND ITS TREATMENT. By WILLIAM P. SPRATLING, M.D., Superintendent at the Craig Colony for Epileptics at Sonyea, New York. Octavo of 522 pages. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

It is indeed a pleasure to review this work, which is the result of an experience of nearly ten years. No better opportunity could be offered to study epilepsy than the author has had as medical superintendent of the Craig Colony for Epileptics at Sonyea, N. Y. The old classification of epilepsy, based on symptomatology, is adopted. Etiological classification is practically hopeless. The influence of heredity as a causal factor is insisted upon, and the symptoms of the various forms of epilepsy are given in detail. The author makes the statement that practically 5 per cent. of epileptics are possibly curable, and that, if all cases would come under treatment early in the disease, this number would be doubled or trebled. This percentage is greater than the experience of most neurologists would teach, for we are too prone to believe that epilepsy is an incurable disease. The author, however, is not alone in his view, for he quotes G. Aldren Turner, who regards 10.2 per cent. of epileptics as curable. The chapter on the pathology is by T. P. Prout and L. P. Clark. These authors incline to the view that epileptic convulsions are a manifestation of a diseased state of the sensory elements of the cortex. They base their views largely on the experimental investigations of Prus and others. In these experiments the pyramidal fibres were cut, but on cortical electric excitation convulsions were obtained. On cutting all of the fibres except the motor, electric stimulation did not produce convulsions. Prout and Clark examined twenty epileptic brains and found diffuse cortical changes, especially in the second cortical layer of cells, the cells of the sensory type. The alterations were nuclear. They argue that the destruction of these cells leaves the motor cells indefinitely informed of the sensation which they should normally respond to, and that this causes an overaction of the motor cells. This is a very ingenious theory, but is hardly borne out by pathological facts as definitely as the authors assume. The cellular changes in epilepsy have been repeatedly studied, but such alterations as the authors described are by no means constant and their conclusions can hardly be accepted. In the treatment the author strongly insists upon the treatment of the patient himself instead of the disease, and believes that colony life is the best. Of drugs bromides have been of most use. The book is well put up and is an admirable presentation of the present knowledge of the subject. T. N. W.

DIET IN HEALTH AND DISEASE. By JULIUS FRIEDENWALD, M.D., Clinical Professor of Diseases of the Stomach in the College of Physicians and Surgeons, Baltimore; and JOHN RUHRAH, M.D., Clinical Professor of Diseases of Children in the College of Physicians and Surgeons, Baltimore. Octavo volume of 689 pages. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

The influence of diet and hygiene upon pathological as well as physiological processes is being daily more and more recognized by the profession, and with the advance in our knowledge of metabolism the study of dietetics is steadily assuming an increasingly important role.

The latest addition to the literature of this subject has been made in the form of a text-book on *The Diet in Health and Disease*, by Friedenwald and Ruhräh. The subject is considered under the following headings: The Chemistry and Physiology of Digestion; Classes of Foods; Beverages and Stimulants; Various Factors in their Bearing on Diet; Infant Feeding; Diet for Special Conditions; Special Methods of Feeding; Diet in Disease—each being treated of seriatim; Special (diet) Cures; Management of Surgical Cases, etc. The foregoing topics are discussed in a concise and most satisfactory manner from a practical point of view, and are followed by numerous standard diet lists which have weathered the test of trial in public institutions, armies, navies, etc. There is also an extensive number of recipes for preparing food, tables of food composition, and a section devoted to the much mooted topic of food adulteration and resultant disease.

We take pleasure in most highly recommending the work for its excellence of arrangement, latitude of subject, and practical utility. G. W. N.

Atlas of the External Diseases of the Eye. By Prof. Dr. O. Haab, of Zurich. Second edition, thoroughly revised. Edited, with additions, by G. E. de Schweinitz, A.M., M.D., Professor of Ophthalmology in the University of Pennsylvania. With 98 colored lithographic illustrations on 48 plates, and 232 pages of text. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

This atlas deserves a place in the library of all practitioners, especially those who have been denied the privileges of frequent observations of external ocular affections.

The editors are men of such wide clinical experience and keen powers of observation that any volume emanating from them is assured a most hearty greeting.

Beginning with the inspection of the eye, the student is shown the various methods of obtaining the data so essential to a complete examination of this organ.

Following this, the lacrymal apparatus, lids, conjunctiva, cornea sclera, iris, ciliary body, lens, vitreous, glaucoma, and diseases of the orbit are successively dealt with.

The text freely conforms to the intentions of the volume, being definite and concise, and is generously illustrated with beautiful and accurate chromolithographic plates. Associated with each plate is a brief clinical history and explanatory notes.

Throughout the text the editor has inserted a number of useful and valuable additions which are indicated by brackets.

In the second edition the work has been thoroughly revised and reference made to a number of the worthy modern therapeutic agents.

Eight new chromolithographic plates have also been added. Of these, those illustrating trachoma, spring conjunctivitis, ulcerating eczema, pustules of the cornea, and staphyloma are most likely to be of greatest service to the average student. T. B. H.

A Text-book of Legal Medicine and Toxicology. Edited by Frederick Peterson, M.D., and Walter S. Haines. In two volumes. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

This system of two volumes with thirty-seven contributors has all the virtues and many of the defects of a system. No change has been made in the articles contributed, and this has led to some parts of the subject being covered in different parts of the book. The same subject is often separated, parts of the subject of insanity, for instance, being in Vol. I. and parts in Vol. II. In reviewing a book of this kind, each subject should be considered separately. Inasmuch, however, as lack of space precludes us from doing this, some of the articles deserving attention will be considered.

In the first volume the articles are uniformly excellent. "The Technique of Medico-legal Post-mortems," by Hektoen; "Death and Injuries by Lightning," by Jelliffe; "Gunshot Wounds," by Hall; "Inebriety," by Hammond, and "Railway Injuries," by Da Costa, deserve special commendation. The article on "Inebriety," by Hammond, deals with the legal side of the subject of alcoholism in a clear and comprehensive manner. Hall has contributed much original work in his article on "Gunshot Injuries."

In Vol. II. the subject of Toxicology is treated by Haines, Holland, Prescott, Hunt and Jones, Doremus and Harrington in a very thorough and lucid manner. The knowledge of this department, including recent reviews of the different tests, has been included and thoroughly digested.

The article by Vaughan, on "Post-mortem Imbibition of Poisons," deserves commendation as an excellent digest of the subject. The same may be said of the "Medico-legal Examination of Blood and Blood Stains," by Wood.

The subjects relating to marriage, pregnancy, abortion, etc., are, as a rule, well done, but the reviewer must take exception to the tenor of the article on infanticide. Inasmuch as this is a text-book of legal medicine, the legal aspect of the subject should be kept in mind. The definition of infanticide is given as follows: "Strictly speaking, infanticide is the intentional destruction of the newborn child and the destruction of the fœtus during birth." From a legal standpoint, infanticide is considered as such a crime after the child has left the mother's body. Cases are cited to show the uselessness of the hydrostatic test. The hydrostatic test is not so much of value as a negative sign as it is when present and of positive value as to live birth. The cases reported in this article do not invalidate the hydrostatic test as a useful method of procedure, but merely serve to point out the deficiency of this test, which, when controlled by microscopic investigation, is of much value.

The book will be of more value as a reference work for lawyers and doctors interested in court work than as a text-book for students.

The binding, paper, illustrations, and indexing are all that could be desired in a work of this kind.

D. J. McC.

Saunders' Medical Hand Atlases. Operative Gynecology. By W. Oskar Schaeffer. Authorized translation from the German, with editorial notes and additions. Edited by J. Clarence Webster. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

This little book contains 131 pages and is divided into ten chapters. The first eight chapters are devoted to plastic work and to operations by the vaginal route. In the chapter devoted to the repair of incomplete lacerations of the perineum the following operations are recommended in the order given: Hager's, Bischoff's, Freund's, von Winckel's, A. Martin's, and the Lawson-Tait flap-splitting. The absence of the Emmet operation is very noticeable; so throughout the book the best German operative views are carefully given, and but very little attention has been paid to the American views. Chapter IX. is devoted to operations on the genital organs that require cœliotomy. This chapter contains but fourteen pages. Chapter X. is devoted to the Alexander-Adams operation for stitching the round ligaments in cases of retrodisplacement of the uterus. No directions are given as to the disposal of the round ligaments after suture. The book is freely and well illustrated. There are 42 colored lithographic plates and many text illustrations. For one wishing to study the German methods of operating, and especially the methods of W. Schaeffer, the book will be an excellent one, but it does not seem likely that the work will be of much practical value to the average gynecologist or physician in this country. C. C. N.

POST-GRADUATE COURSE

DEPARTMENT OF MEDICINE

UNIVERSITY OF PENNSYLVANIA

COURSES OFFERED TO GRADUATES IN MEDICINE DURING THE MONTHS OF MAY AND JUNE, 1905

ANNOUNCEMENT

The course will extend over a period not exceeding six weeks.

Beginning May 15, 1905, the University will conduct a spring course in Medicine, designed especially for practitioners, but open also, in the laboratory courses, to advanced students in Medicine. It embraces almost the entire curriculum of Medicine, and has been devised to meet the requirements of a wide group of practitioners and students of Medicine.

In designing the instruction offered in the spring course, the needs of the practitioner have been kept in view, and so far as possible the work has been made of purely practical character. While this feature is emphasized in the clinical branches and specialties, it has not been lost sight of in the laboratories. In all the courses the work is of a nature to appeal to the surgeon and general practitioner who wish to revive or complete their knowledge of certain subjects, and to advanced students in Medicine who may not have had opportunities to pursue these courses of study.

The number of attendants upon certain clinical courses will be necessarily limited, in order that close personal attention may be accorded the patients. This number will vary with the nature of the course; and the admission, under these circumstances, will be made in the order of application.

The schedule of hours for post-graduate study is so arranged that a comprehensive course may be taken without conflict of hours, and for this purpose the subjects have been divided into two groups:

Group I. is devoted entirely to Internal Medicine, including laboratory and clinical work, and to the following specialties: Pediatrics, Neurology, Ophthalmology, Otology, Rhinology, and Laryngology.

Group II. is devoted entirely to General Surgery, including Surgical Anatomy and Pathology, and to Gynecology, Obstetrics, Orthopedic Surgery, Genitourinary Diseases, and Dermatology.

To those, however, who are desirous of devoting more time than is allotted on the schedule to any one subject, special courses and opportunities are offered for more advanced work.

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3. Medical Clinic, or Bedside Instruction. Dr. Stengel, University Hospital, Mondays at 12 noon.
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6. Clinical Medicine, with Especial Reference to the Diagnosis and Treatment of Diseases of the Gastrointestinal System. Dr. Steele, University Hospital, Mondays at 1 P.M., and Saturdays at 12 noon.
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1. Clinical Instruction in the Diseases of Children. Drs. Griffith and Ostheimer, in the Wards of the University Hospital, on Wednesdays at 1 P.M., throughout the course.
2. Feeding in Infancy. Dr. Thompson S. Westcott, on Mondays and Fridays, in the Amphitheatre of the Children's Hospital, from 4.15 to 5.15 P.M., throughout the course.

This course will include the Modification of Milk. The Calculation of Percentage Formulæ. General Considerations of Substitute Feeding. Practical Application of Percentage Feeding. Weaning. Feeding in Difficult Cases. Dietetic Treatment of the Chronic Gastrointestinal Catarrhs. Various Expedients Necessary in Special Cases. Differential Modifications of Proteids, etc. Use of Cereal Preparations, Condensed Milk, etc. Clinical Cases Illustrating Nutritional Diseases: Rickets, Scurvy, Atrophy, Tuberculosis, Syphilis, and their Dietetic Management.

SURGERY

1. Clinical Surgery. University Hospital, daily at 1 P.M., including operations in the Surgical Clinic, Surgical Diagnosis, Ward Rounds, and Demonstrations of the Modern Methods of Administering Anæsthetics.
2. Surgical Pathology. Dr. Müller, Tuesdays and Thursdays, from 11 A.M. to 1 P.M., at the New Medical Laboratories. This course consists in the demonstrations of the gross and microscopic lesions of the more common surgical affections, in so far as they apply to diagnosis and treatment.
3. Operative Surgery on Cadavers and Animals. Dr. Carnett, Mondays and Fridays, 11 A.M. to 1 P.M. This course will include Intra-abdominal Operations upon Animals (operations upon the Stomach, Gall-bladder, and Intestines), and such operations upon the Cadaver as cannot be demonstrated to advantage upon the Living Animal. The course will be arranged in accordance with the special needs of the Student. (Limited to ten.)
4. Surgical Anatomy. Dr. Davis. Mondays and Fridays, 2 to 3 P.M., Logan Hall. With especial reference to the anatomy of the peritoneal cavity, of fractures and dislocations, including demonstrations of methods of reducing dislocations.
5. Skiagraphy, Radiotherapy, and Phototherapy. Dr. Pancoast. Mondays, Wednesdays, and Fridays, 9 to 11 A.M. *X*-ray Department, University Hospital. Preliminary instruction in the various parts of an *x*-ray equipment, the handling of the apparatus, and in the principles of electric currents used in the production of the *x*-rays. This will include also the dangers in their application, their effects upon healthy and diseased tissues, and the methods of protection to the patient and operator. Instruction in the technique of radiographic exposures and the development of plates in the dark room. The therapeutic application of *x*-rays, with technique required for treating various pathological conditions, with demonstrations by treatment of patients. The therapeutic use of Finsen rays and "High Frequency Currents."
6. Orthopedic Surgery. Orthopedic Clinic, Dr. Willard, Tuesdays, 12 to 1; Drs. Young, Spellissy, and Reed, Mondays, Thursdays, and Fridays, 12 to 1; Operations, Lectures, Demonstrations, and Practical Work in the Orthopedic Ward and Dispensary. The Special Orthopedic Gymnasium for the Treatment of Paralyses, Deformities, Curvatures, etc., is open daily from 12 to 2.
7. Pediatric Surgery. Dr. Jopson. Wednesdays and Saturdays, Children's Hospital, 11 A.M. to 1 P.M.
8. Genitourinary Diseases. Drs. Neilson and Stier. In the Out-patient Department of the University Hospital, Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1. This course is altogether practical, and covers the following subjects: Venereal Diseases, Surgical Diseases of the Genitourinary Organs, the Use of Instruments for Diagnosis and Treatment of Diseases of the Urethra and Bladder, and demonstration of operative procedures.
9. Minor Surgery. Dr. Norris, University Hospital, daily from 12 to 1 P.M.

GYNECOLOGY

1. Gynecological Clinic. Dr. Clark. Wednesdays and Fridays, 2 to 4 P.M., University Hospital. The practical work in this course will be limited to five graduate students.
2. Gynecological Clinic. Dr. Beyea. Tuesdays and Thursdays, 11 A.M. to 1 P.M., Gynecean Hospital.
3. Gynecological Pathology Dr. Anspach. Hours to be arranged for the convenience of those taking the course. (Limited to ten.)

OBSTETRICS

Dr. Hirst and assistants. Tuesdays and Thursdays, 3 to 4 P.M., in the Maternity Pavilion of the University Hospital. This course consists in demonstrations of the Surgical Treatment of the Injuries of Childbirth by Primary, Intermediate, and Secondary Operations; Treatment of the Pelvic and Abdominal Complications of the Child-bearing Process by Pelvic and Abdominal Surgery; the Obstetrical Operations, Obstetrical Diagnosis, and Preliminary Examination of the Patient, and the Management of the Puerperium.

DERMATOLOGY

Dr. Hartzell. Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1 P.M. This course is given in the Out-patient Department of the University Hospital and Wards of the Philadelphia Hospital, and will be devoted to the Examination, Diagnosis, and Treatment of patients in daily attendance at the clinic.

NEUROLOGY AND PSYCHIATRY

1. Clinics. Dr. Mills on Mondays and Dr. Spiller on Tuesdays and Thursdays, 3 P.M., at the University or the Philadelphia Hospital.
2. Neuropathology. Dr. Spiller will give practical instruction either by the lantern or in the laboratory once a week for those desiring to take Neuropathology in connection with the clinical work.
3. Electrotherapeutics and Ward Class Demonstrations. At least once a week, by Dr. Potts and assistants, University Hospital.
4. Psychiatry. Dr. Burr. Instruction in Mental Diseases either by lectures or by ward class demonstrations, Wednesdays and Fridays, 3 P.M., Philadelphia Hospital.
5. Special Course. The course announced above is open to all students of the post-graduate department. Any student wishing to take Neurology and Psychiatry as a special subject, or in combination with one or two other subjects, can make arrangements with the Dean of the Faculty and the Teachers in the Neurological Department for the fuller course.

OPHTHALMOLOGY.

This course is designed for those who are especially interested in the eye, and is limited to ten.
1. Operative Clinic. Dr. de Schweinitz, Thursday, 3 to 4 P.M., University Hospital.
2. External Diseases of the Eye, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 3 to 4 P.M.
3. Operations on Animals' Eyes, Dr. de Schweinitz, assisted by Dr. Mellor, Tuesdays, 4.30 to 5.30 P.M.
4. Functional Testing of the Eye, including the principles of Refraction, Muscle-balance Testing, Retinoscopy, and Ophthalmometry. Dr. Carpenter, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 2 to 3 P.M.
5. Pathological Histology. Dr. Shumway, Mondays, Wednesdays, and Fridays, 4 to 6 P.M.

OTOLOGY.

Dr. Randall. (*a*) Daily Clinics at the University Hospital. (*b*) Instruction in the Anatomy of the Ear by means of lantern demonstrations and anatomical preparations in connection with the Wistar Museum of Anatomy.
In demonstrating operative procedures, it is expected that either clinical material or cadavers will be used.

LARYNGOLOGY.

Dr. Grayson. Daily in the Laryngological Clinic of the University Hospital, at 2.30 P.M. A course in Instrumental Technique and in the Diagnosis and Treatment of Diseases of the Nose and Throat. The microscope will be used to supplement the clinical diagnosis of neoplasms and exudative inflammations, and in the treatment. Instruction will be given in the ordinary methods of local therapeusis, but opportunities will be offered to perform the various operations for deflection of the nasal septum, for the removal of polyps, the faucial tonsils, adenoid growths, etc.
Note.—Those desiring to take the course in both Otology and Laryngology may take these subjects on alternate days.

BACTERIOLOGY AND HYGIENE

1. Elementary Bacteriology. Drs. Gildersleeve, daily, 9 to 11 A.M., in the Laboratory of Hygiene. This course is designed to supply the needs of the practitioner of medicine. It comprehends the preparation of culture media, the methods of sterilization, the methods of isolation and study of bacteria in pure culture, the study of the best known and most important of the pathogenic species, the methods of disinfection, the use of the microscope, and the methods of staining employed in bacteriological work.
2. Advanced Work in Bacteriology. Dr. Bergey, daily, 9 to 11 A.M., in the Laboratory of Hygiene. This course will be arranged in accordance with the qualifications and inclinations of each individual student.
3. Practical Hygiene. Dr. Bergey, 9 to 11 A.M., daily, in the Laboratory of Hygiene. Applicants for the course must possess a working knowledge of quantitative chemical analysis. The course covers exercises in the physical and chemical study of the atmosphere, with methods of recording results; studies in ventilation and heating, and methods for estimating extent of the same; physical, chemical, and bacteriological study of water; the artificial and natural methods of water purification; pollutions to which water is liable; interpretation of results of analysis; studies of milk from the sanitary standpoint; sanitary food inspection and analysis.

CHEMISTRY

1. Analysis of the Urine. Drs. Marshall, D. W. Fetterolf, Ryan, and Hawk. Tuesdays and Thursdays, 9 to 11 A.M., Robert Hare Chemical Laboratory.
2. Toxicology. Tuesdays and Thursdays, 9 to 11 A.M., Robert Hare Chemical Laboratory.
3. Elementary Physiological Chemistry. This course will consist of a systematic study of the carbohydrates, fats, proteids; salivary, gastric, and pancreatic digestions, and of the bile, milk, and blood. If desired, work will be given in tissue chemistry and in general food analysis. (This course will only be given in the event of there being at least six students.)

ANATOMY

1. Embryology. Dr. Piersol. Tuesdays, Thursdays, Saturdays, 9 to 11 A.M., Logan Hall. 2. Microscopic Technique. Drs. Piersol and Formad. 3. Practical Anatomy. Dr. G. Fetterolf.

PATHOLOGY

Drs. Smith, Loeb, and C. A. Alburger. 1. Autopsy-making. 2. Selected Experimental Pathology. 3. Elementary Pathological Histology. 4. Advanced Pathological Histology. New Medical Laboratories. (This course will not be given to classes of less than six.)

PHYSIOLOGY

Drs. Reichert and Lodholz. 1. Elementary Course in Practical Physiology. 2. Advanced Course in Practical Physiology. (These courses will not be given to classes of less than six.) Hours to be arranged to suit the convenience of those taking the courses. New Medical Laboratories.

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UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. I of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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Edward T. Reichert, M.D., Professor of Physiology.

Barton Cooke Hirst, M.D., Professor of Obstetrics.

J. William White, M.D., John Rhea Barton Professor of Surgery.

George A. Piersol, M.D., Professor of Anatomy.

John Marshall, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology.

Louis A. Duhring, M.D., Professor of Dermatology.

Alexander C. Abbott, M.D., Pepper Professor of Hygiene and Bacteriology.

John G. Clark, M.D., Professor of Gynecology.

George E. de Schweinitz, M.D., Professor of Ophthalmology.

Charles H. Frazier, M.D., Professor of Clinical Surgery, and Dean of the Faculty.

Allen J. Smith, M.D., Professor of Pathology.

De Forest Willard, M.D., Professor of Orthopedic Surgery.

B. Alexander Randall, M.D., Clinical Professor of Diseases of the Ear.

J. P. Crozer Griffith, M.D., Clinical Professor of Diseases of Children.

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William G. Spiller, M.D., Professor of Neuropathology and Associate Professor of Neurology.

Charles W. Burr, M.D., Professor of Mental Diseases.

M. Howard Fussell, M.D., Assistant Professor of Medicine.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

ABSTRACT OF A PAPER UPON THE ACTION OF ALCOHOL UPON THE CIRCULATION.

By Horatio C. Wood, M.D., LL.D.,
Professor of Materia Medica, Pharmacy, and General Therapeutics, University of Pennsylvania,

and

Daniel M. Hoyt, M.D.,
Assistant Demonstrator of Pharmacodynamics, University of Pennsylvania.

At the April meeting of the National Academy of Science an elaborate research upon the action of alcohol upon the circulation was read by the authors above named. This research, for which work a sum of money had been appropriated from the Bache Fund of the National Academy, will be published in full in the *Memoirs* of the Academy. We are enabled to lay before our readers the following abstract of the ground covered and the results obtained.

In the introduction to the research, attention is called to the facts that probably since the days of Noah, and it may perchance be since the days of early Egypt, the popular belief has been that alcohol is a stimulant to the circulation, and that this belief has been shared by the great mass of clinicians from the beginning almost up to the present day: that there has, however, arisen a divergency of opinion among competent pharmacologists as to the action of the drug upon the circulation, so that at present there are two distinct schools, in the one of which it is taught that alcohol is a stimulant to the heart and to the circulation; in the other that the only action of alcohol upon the circulation is that of a depressant, moderate doses of alcohol having no direct action upon the blood movements, though at times, by irritating the gastric mucous membrane or other part, they may seemingly excite the heart. Again, in this introduction, the authors state that the literature of the subject has been so thoroughly studied by competent authorities that further discussion of it seems a mere waste of time; and that anyone desirous of looking up the matter will find a discussion of the literature from the two points of view in Prof. Abel's articles in vol. ii., page 91, of the *Physiological Aspects of the Liquor Problem*, published by Houghton, Mifflin & Co., and in Wood's *Treatise on Therapeutics*, the twelfth edition of which is now nearly through press. For these reasons in the memoir now abstracted there is no general discussion of the alcohol literature.

The second part of the memoir by Drs. Wood and Hoyt is given to the detailing of the experimentation upon the subject. In the experimentation both Drs. Wood and Hoyt took part, and each of them is equally responsible for the experimental results and their records. The experiments are arranged in series, and will be published with full details.

ANIMAL EXPERIMENTATION.

The experiments made with alcohol upon the lower animals had for their intent the finding out of certain facts, and therefore naturally arrange themselves into series; each series being directed to the discovery of an individual fact, or of several facts closely allied. These series are:

(1) Experiments made upon the uninjured animal to determine the effect of alcohol upon the arterial pressure.

(2) Experiments made upon dogs suffering from an infective fever to determine whether alcohol acts under these circumstances as it does upon the normal animal.

(3) Experiments made upon dogs with variously situated sections of the spinal cord in order to determine the effect of alcohol upon the arterial pressure, when the general vascular system has been separated from its dominant vasomotor centres.

(4) Experiments as to the effect of alcohol upon the arterial pressure, after the aorta has been tied in the middle thoracic or upper abdominal region.

(5) Experiments upon normal dogs with the Ludwig stromuhr to determine the effect of alcohol upon the rate of the blood flow.

(6) Experiments to determine the influence of alcohol upon the isolated reptilian heart.

Series First. In this series two sets of experiments were performed, those in which the alcohol was given by inhalation and those in which it was administered in the more usual way of intravenously.

In the inhalation experiments the method adopted was to allow the dog to breathe through a tracheal tube which was connected with a double-tube bottle in such way that the air had to bubble through a considerable mass of 80 per cent. alcohol. It was found that under these circumstances the air was loaded with the vapor of alcohol, while an abundant supply of oxygen was furnished the animal. Usually the inhalation was not accompanied by any struggling or excitement, but it was not found possible to produce a complete anæsthetic unconsciousness. This was contrary to the result reached many years ago by H. C. Wood, that animals

could be anæsthetized with simple alcohol placed in an imperfectly closed inhaler.

It is evident that the anæsthesia which was produced in the earlier experiments of Wood was largely the outcome of a slow asphyxiation due to an imperfect supply of air. Alcohol when given in the method adopted in the present series of experiments usually failed to produce rise of the arterial pressure, and in the exceptional case only caused such rise very late in the poisoning, at a time when the respiration had been profoundly affected by pulmonary congestion and œdema due to the local action of the alcohol upon the pulmonic mucous membranes. At such times the pulse was slow and full, and it was evident that the circulatory changes were the outcome of asphyxiation. In most of the experiments the animal died suddenly by respiratory failure, there either being no unconsciousness until the act of death had been entered upon or was about to begin.

Series Second. The next series of experiments were directed simply to studying the effect of the intravenous injection of alcohol upon the circulation in the normal dog. In all of the experiments ether was used for the preparation of the artery and vein, care being taken to allow the effects of the ether to go off before the first record of blood pressure. In a few instances a small amount of morphine was also given to the animal operated upon.

In the series of experiments made by intravenous injection of alcohol the results were varying. Sometimes no effect was produced until the alcohol had been given in sufficient amounts to reduce the pressure; in other cases a slight rise of pressure was obtained, and in one case a very distinct rise. The experiments appear to show that small doses of alcohol have a tendency to cause in the normal dog a slight rise in the arterial pressure, but that this tendency is not pronounced and often fails to show itself even when carefully calculated doses are employed. Large doses of alcohol always lower blood pressure.

Two experiments were made upon dogs suffering from distemper accompanied with the usual systemic symptoms and pronounced fever. In one of these experiments alcohol produced no rise of the arterial pressure; in the second experiment a slight but distinct rise was secured, so that it would appear that in the dog suffering from the general prostration and circulatory disturbance of an infective fever alcohol will sometimes cause a rise of blood pressure, but has no consistent, pronounced influence in so doing. The drug therefore seemingly acts upon the circulation in fever in no way differently from that in which it acts upon it in health.

A remarkable effect noted in these dogs, not connected with the circulation, was the influence of the alcohol upon the nervous system, an influence so pronounced as to suggest that very possibly in human fever alcohol is of service as a calmative agent. The animals were suffering from fever and its discomforts; were of necessity restrained in the ordinary dog trough; were violently restless and howling at the time of the intravenous injection of the alcohol. The alcohol was not given in sufficient dose to produce a recognizable narcosis, yet within two or three minutes after its injection the animals became perfectly quiet and apparently blissfully content.

Series Third. In the experiments included in this series the spinal cord was always cut somewhere in the cervical region, artificial respiration being maintained. Every effort was made to keep uniformity of rate and activity in the respiratory movements, and in nearly all the experiments the condition of the cord was tested by the effect of asphyxiation upon the circulation, so that it was physiologically demonstrated that the vasomotor system was completely paralyzed. When no physiological test was made the completeness of the section of the cord was confirmed by post-mortem examination. The section of the cord is a surgical procedure requiring so much cutting and time, and involving so much suffering that the animal was perforce thoroughly anæsthetized during the surgical procedure; but in every experiment after the operation time was allowed for the effects of the anæsthetic to disappear so that the conjunctival reflexes were normal.

An inspection of the records of these experiments, which will appear in the *Memoirs* of the National Academy, will show that in Experiment 7, in which the dog was young and vigorous, the arterial pressure was raised by alcohol over 100 per cent. in spite of the consentaneous marked decrease in the rate of the pulse; that in Experiment 8 the pressure was raised about 25 per cent. at the maximum, in spite of the fact that there had been a great deal of hemorrhage during the operation; that in Experiment 9 the pressure was elevated as much as 50 per cent. at the maximum, the pulse being reduced in frequency; that in Experiment 10, where there was much hemorrhage, the elevation of pressure at the maximum was about 25 per cent.; that in Experiment 11 the maximum rise of pressure was about 40 per cent.; that in Experiment 12 the maximum rise of pressure under the use of alcohol was about 50 per cent.

In none of these cases was the arterial pressure kept at the highest point for a great length of time, but there was always a prolonged maintenance of the pressure above the normal.

Series Fourth. In series four of the experiments the effort was made to study the action of the alcohol upon the blood pressure after tying of the abdominal aorta, but the results obtained were entirely unsatisfactory, because of the enormous disturbance of the respiration and of the general system produced by the operation. There was so much unrest and motion and the circulation was so irregular that the results are probably of no value as throwing light upon the action of alcohol upon the circulation. These experiments ought to be repeated upon curarized dogs, with artificial respiration, if any weight at all is to be attached to them. Under the best circumstances, however, the conditions are so abnormal that it did not seem to the investigators that any results reached

would be of importance, and the experiments were not carried to a further conclusion.

Series Fifth. The fifth series of experiments were made with the *stromuhr*. Some practical difficulties were found in the use of this instrument, these difficulties being chiefly connected with the prevention of the coagulation of the blood in the small tubes. Peptones were tried without satisfactory results; neither leech extract nor the active principle of the salivary gland of the leech was to be had in the American market, and the method of Franz, for unknown reasons, did not bring the desired results in the hands of the experimenters. The method of preparing the leech extract which was finally hit upon will be given in full in the *Memoir*.

Three experiments with the *stromuhr* are recorded in the *Memoir*. In Experiment 16, under the influence of 8 c.c. of 25 per cent. alcohol, there was a decrease in the time required to fill the stromuhr from twenty-one to fourteen seconds, or, in other words, an increase of 33 per cent. in the rapidity of the flow of blood. This increase in the rapidity of the flow of blood was maintained after the further injection of 5 c.c. of alcohol, but gradually lessened on the repetition of the dosage, so that after 36 c.c. of the alcohol it had practically disappeared. The paralyzant influence of the alcohol then became more and more apparent, and when 45 c.c. in addition to that previously used had been injected the rate of flow through the artery was less than half of the normal.

In Experiment 17, in a dog weighing 8 kilos, 9 c.c. of alcohol reduced the time necessary for the filling of the *stromuhr* from twenty-two to fourteen seconds, *i. e.*, increased the rapidity of the blood flows a little over 33 per cent. It is remarkable that the further injection of 35 c.c. of alcohol had no further effect upon the rate of the blood current, but when 12 c.c. additional were subsequently given the flow came to about the normal.

Experiment 18 was a more complicated one than the others. In it the blood pressure was studied at the same time as the rate of blood flow. The administration of 1 c.c. of alcohol brought down the time necessary for the filling of the *stromuhr* from thirty-five to fifteen seconds; in other words, more than doubled the rate of flow. When 6 c.c. of additional alcohol had been given the increase of the rate of flow decreased until finally the paralyzant effect of the alcohol upon the circulation became very apparent, so that seventy-four seconds were required to fill the *stromuhr* instead of thirty-five, the normal. A peculiarity of this experiment is the extraordinary effect reached by the injection of a very small amount of alcohol. It should be noted, however, that the dog which was experimented upon was not only a very small dog (weight twelve pounds), but that it was also a very young puppy, and therefore presumably abnormally sensitive to the influence of drugs.

Series Sixth. In the sixth series of experiments was studied the action of the alcohol upon the isolated frog's heart. Kroneker's apparatus was first employed, but with it no constant effect was demonstrated as produced by the alcohol, except that after large doses the cardiac movements were distinctly lessened. For reasons which are given in full by the investigators the conclusion was reached, however, that the Kroneker apparatus is not applicable to the study of pharmacological problems. Experiments were then made with the Williams apparatus; records of these experiments will show that in Experiment 19 the exhibition of $\frac{1}{4}$ per cent. of alcohol was followed by a distinct fall of the arterial pressure; that in Experiment 20 the use of 1 per cent. of alcohol was followed by a temporary rise, soon giving way to a distinct fall, which became more accentuated when 3 per cent. of alcohol was used; that in Experiment 21 $\frac{1}{4}$ per cent. of alcohol apparently produced a very decided and persistent rise of heart work, which lasted until the alcohol was increased to 1 per cent., when there was a pronounced fall, not, however, below the normal; while later 5 per cent. of alcohol decreased the heart work to below the normal; that in Experiment 22 the heart work was distinctly and persistently increased by the exhibition of $\frac{1}{4}$ per cent. of alcohol, the increase being maintained for over half an hour, until the exhibition of $\frac{3}{4}$ per cent. of alcohol produced a fall below the normal.

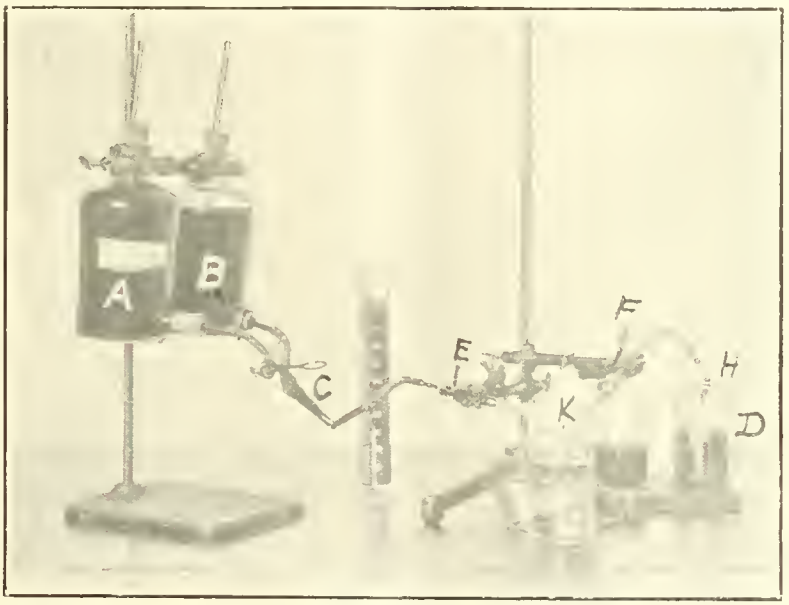
On the whole, these experiments seemed to the investigators to indicate that in small doses alcohol increases the work of the isolated frog's heart, but the results obtained were distinctly discordant and unsatisfactory. In all these experiments the hearts of small frogs were used, and after much experience with Kroneker's apparatus, Williams' apparatus, and the one shortly to be described, it became apparent that experimental results by the use of small hearts are not reliable. The resistance in either the Kroneker or the Williams apparatus, when the small heart is used, is out of all proportion to the cardiac power, and feeble muscle fibre may well stretch, give way, or lose functional ability rapidly under the the strain. Moreover, in the Williams apparatus, when the heart is small it is difficult to avoid injury to it in the insertion and securing of the cannula in the truncus arteriosus, and we know of no way of judging with certainty whether the heart has or has not been injured. Whatever the reasons may be, of this fact we are confident, namely, that even with the best forms of "frog's heart apparatus," if the experimental results are to be persistent in the one experiment, and consistent in the various experiments, it is essential that the heart of very large bullfrogs, or of large snakes, or tortoises, be employed. We believe that the failure to obtain a rise in Experiment 19 from the $\frac{1}{4}$ per cent. of alcohol was probably due to injury of the heart in the making of the preparation.

Led by the difficulties inherent to the older forms of apparatus, Wood and Hoyt devised and used an apparatus which is a modification of the Williams' apparatus. This apparatus consists, beginning at the left, in a pair of Mariott bottles, united by a Y-shaped tube, with a clip so arranged as to shut off either bottle at will. Then, of the ordinary Williams apparatus with the modification that at the distal

end, beyond the second valve F, the blood is allowed to pass through a glass tube and to drop into a beaker-glass for a fixed period of time. In using this apparatus the pressure upon the heart can be varied by elevating the bottles A and B, and the resistance to the systole by elevating the drip-tube H. It was found in practice that the elevation to the bottles and to the drip-tube must have such relation that the drip-tube shall be at least as high as the pressure point in the bottles.

Our experience shows that in order to get the best results with this apparatus some care and experience are necessary in so adjusting the height of the reservoir bottles above the heart that the amount of pressure upon the heart during diastole and the amount of resistance to the heart during systole shall be properly proportioned to the size and power of the organ. In the frog and probably other reptiles the internal diastolic cardiac pressure is very slight, so that in the isolated heart it is very easy to have conditions both during diastole and systole which are entirely unnatural.[1]

The records of the experiments made with the modified Williams apparatus show that in Experiment 23, under the influence of ¼ per cent. of alcohol, the heart work increased from a maximum of 105 to 150 c.c., then on the withdrawal of the alcohol fell to 84 c.c., but rose again to 111 on the renewal of the alcohol, to fall again to 100 when the alcohol was withdrawn; to rise to 110 again when the alcohol was added in 0.5 per cent., this rise being followed, however, by a rapid fall in the amount of the heart work, which on the increase of the alcohol in the blood to 1 per cent. came down to 43 c.c. per minute. The technical details of this experiment were not satisfactory in that at one time the apparatus had to be taken entirely apart on account of coagulation of blood in it, and that later the process had to be again stopped in order to remove air which had been shut in the tube.



A and B. Mariott bottles used as reservoir. C. Tube through which the nutrient liquid is carried past the valve *E* to the heart at *K*, to be pumped thence through the valve *F* to the drip-tube *H*, to allow it to fall into the reservoir *D*.

In Experiment 24 the work of the heart rose from 19 c.c. during the prealcoholic period to 91 c.c. during the alcoholic period, falling very distinctly when the alcohol was withdrawn from the blood; increasing later to 104 when the alcohol was increased to 0.5 per cent. and falling rapidly to 22 when the alcohol was withdrawn; rising again on the addition of 1 per cent. of alcohol temporarily, the rise being followed by a fall. The first part of this experiment was in its technique not thoroughly satisfactory; the apparatus in the beginning failed to work properly for reasons which were not clearly made out, but requiring ten minutes for taking everything apart and getting the tubes together again before the blood flowed freely. The original normal may have been incorrect, but the subsequent readings were clearly accurate.

The two experiments 23 and 24, whose results we have just epitomized, were made with rather small hearts derived from frogs of corresponding size. For reasons which have

[1] In trials with the pure Ringer solution as a nutrient fluid, fatigue developed so rapidly as in the opinion of the investigators to make trustworthy results impossible. The fluid which was finally used was similar to that originally employed by Williams, except in the substitution of bullocks' for rabbits' blood. It consisted of a mixture of one part of defibrinated bullocks' blood to two parts of a 0.5 per cent. saline solution. In order that the heart might have a constant supply of oxygen, in no case was the same blood passed twice through the heart. In one of the large reservoir bottles was placed the pure nutrient fluid containing the required percentage of alcohol, so that by simply changing the clip, without disturbing the pressure or in any way disturbing the heart condition, pure nutrient fluid or alcoholized fluid could be run through the viscus at will. We had some difficulty in working the Williams valve, until the laboratory *Diener*, Henry Bevan, suggested the use of the skin of the frog, which was found, when used fresh, or even after keeping in saline solution, to answer admirably.

been heretofore assigned, it seems to be impossible to get with such hearts satisfactory results, and we therefore do not think that much weight can be given to Experiments 23 and 24.

The remaining experiments of the series were made with powerful hearts, capable of overcoming the resistance and other abnormal conditions of the heart under study.

In Experiment 25, under the influence of $\frac{1}{4}$ per cent. of alcohol, the heart work rose from 93 to 103—that is, 12 per cent.; fell 12 per cent. when alcohol was withdrawn, rose about 5 per cent. under the influence of $\frac{1}{3}$ per cent. of alcohol, fell to 10 per cent. below the original normal when the alcohol was withdrawn; the heart subsequently failing under the influence of $\frac{1}{2}$ of 1 per cent. of alcohol.

In Experiment 26, made with a land tortoise, the normal of heart work was found to be 149 c.c., rising to 175 on the addition of $\frac{1}{2}$ per cent. of alcohol to the nutritive fluid, to fall to 125 when the alcohol was withdrawn.

In Experiment 27, in which a snake was used, the heart-work normal was 60 c.c.; the addition of $\frac{1}{2}$ per cent. of alcohol made it rise to 68 c.c., about 13 per cent.; when the alcohol was withdrawn, the work fell to the original normal, to rise again 15 per cent. on the addition of $\frac{1}{2}$ per cent. of alcohol to the blood; to fall again 10 per cent. below the normal when the alcohol was withdrawn, again to rise temporarily under the influence of $\frac{2}{3}$ per cent. of alcohol; to fall again much below the normal on the withdrawal of the alcohol, again to increase under the influence of $\frac{2}{3}$ per cent. of alcohol 16 per cent., to finally fall when the alcohol was withdrawn.

In Experiment 28, with the large heart of a good-sized snapping turtle, $\frac{1}{2}$ per cent. of alcohol raised the heart work from 177 to 213, a gain of 20 per cent.

In addition to the experiments, the details of which have been given, we have made others with the hearts of large frogs, in which the results reached were entirely concordant with those just tabulated. In no experiment has the alcohol failed clearly and positively to manifest its influence, unless it were in Experiments 7 and 8, heretofore discussed.

The results of all the experiments made clearly establish that when the isolated reptilian heart is placed under conditions as nearly natural as is possible, the amount of blood which it will pump during a fixed period, *i. e.*, the amount of work which it will do, is increased usually from 10 to 15 per cent. by the addition of $\frac{1}{4}$ to $\frac{1}{2}$ per cent. of alcohol to the nutrient fluid. In these experiments it was usually apparent that the increased work was manifested by the increase in the amount of blood thrown out by the heart at one systole, and it appeared to the investigators that the alcohol increases the completeness of the diastole.

CONCLUSIONS.

The facts which the investigators have experimentally determined in regard to the action of alcohol upon the circulation are:

1. In the normal dog alcohol does not usually either in small or large dose distinctly increase the arterial pressure, although occasionally such an effect appears.

2. The action of alcohol upon the circulation in dogs suffering from an infective fever, so far as the blood pressure is concerned, is similar to its influence upon the normal dog.

3. After section of the spinal cord in the cervical region, with maintenance of the respiration, alcohol distinctly and consistently increases the arterial pressure; in other words, alcohol increases arterial pressure after the general vascular system has been separated from its dominant vasomoter centres.

4. (Series 5.) The exhibition of small doses of alcohol increases very markedly the rate of flow of blood through the large arteries, as measured by Ludwig's stromuhr, this increase of rate being consistently maintained under the repetition of the intravenous injection of alcohol until the time comes when the rate of flow gradually lessens until under the paralytic influence of the alcohol it becomes much smaller than its norm. The increase of the rate of flow is in no-wise dependant upon or directly related to the arterial pressure, as it may occur without the pressure being sensibly affected.

5. (Series 6.) Alcohol $\frac{1}{4}$ to $\frac{1}{2}$ per cent. added to nutritive fluid feeding an isolated working reptilian heart markedly and persistently increases the amount of this fluid pumped in a given length of time by such heart; that is, markedly increases the work done by the heart, the withdrawal of the alcohol being followed at once by a corresponding decrease in the heart work. If $\frac{1}{2}$ to 1 per cent. of alcohol be added to the nutritive fluid there may be a primary condition of increase of work, followed often in a few minutes by marked lessening of the work done. Larger percentages of alcohol immediately decrease the activity of the isolated reptilian heart.

The first question which naturally arises at this point is as to how far the above facts which we seem to have established agree with the results obtained by previous experimenters; let us look at this matter *seriatim*.

1. Without more elaborate discussion we think that anyone conversant with the literature of the action of alcohol upon the blood pressure will acknowledge that the general drift of the evidence is in accord with the results which we have reached. Most observers affirm they have been unable to get any increase of the arterial pressure by the use of alcohol, while others allege that they have obtained such increase. Attempts have been made by critics to reconcile these differences by asserting the incompetence of one set of observers, but the more probably correct deduction would be that alcohol does not commonly elevate the blood pressure, but for reasons not always apparent in some cases it does so.

2. We know of no experiments having been made as to the effect of the exhibition of alcohol upon the blood press-

ure in dogs suffering from an infective fever, but the results which we have obtained in dogs are in close concord with those reached by Cabot upon human beings suffering from various infective fevers.

3. The only experiments with which we are familiar other than our own upon the action of alcohol on the arterial pressure after section of the spinal cord are those which were made in or about 1900 by Prof. John J. Abel, of Johns Hopkins University. In these experiments the results were exactly those which we have obtained. In a letter written in 1904 by Prof. Abel to Dr. H. C. Wood, Prof. Abel states that in all his spinal-cord experiments with alcohol great care was taken to see that the section of the cord was complete, and he further states that except in certain experiments, when owing to the animal having been extremely feeble and having suffered from violent hemorrhage during the operation, the blood pressure was almost exhausted before the administration of the alcohol, alcohol always caused distinct elevation of the arterial pressure after section of the spinal cord.

4. In regard to the effect of alcohol upon the rate of the blood flow, the only experimental record in literature with which we are familiar is that of John C. Hemmeter,[1] who in a single experiment found that in the dog the blood flow was increased from 158 mm. per second to 399 mm. per second by the exhibition of alcohol. This single experiment is evidently in accord with the results which we have obtained.

5. In regard to the action of alcohol upon the isolated reptilian heart, much work has been performed by various observers at various times, with results which have been discordant. In our study of the effect of the drug upon the reptilian heart the attempt was made to discover, if possible, the reason for this discordancy. The method of cutting the Gordian knot adopted by some authorities, namely, the assertion that everybody who obtained results different from those which they themselves had reached, directly or by the path of preconceived opinions, did not know how to experiment properly, does not seem to us philosophic. Having, however, exhaustively discussed this subject earlier in this memoir, we now merely state our conviction that the reasons for the discrepancies in literature have been made apparent, and that our results are not exceptional in any way.

The interpretation of the experimental facts which have just been stated does not seem to us difficult. The arterial pressure is the result of the interplay of two antagonistic forces, the propelling power derived from the heart and the frontal resistance offered by the bloodvessels. If either of these forces be increased—that is, if the bloodvessels be narrowed or the heart power augmented—the arterial pressure will rise. If either of these forces be diminished, the arterial pressure will fall. If one of these forces be increased and the other diminished, the arterial pressure may rise, may fall, may remain as it has been, according as the balance between the two forces rises, falls, or is maintained. The fact, therefore, that alcohol does not constantly elevate the blood pressure is no proof that it does not stimulate either the heart or the bloodvessels, since it is evidently possible that it may stimulate one dominant factor of the blood pressure and depress the other so equally as to maintain the balance. Further, the fact that the influence of alcohol upon the blood pressure is not a constant one suggests the probability that it does disturb the dominant blood-pressure factors, and is unable always to accurately keep the balance between the two altered forces.

The second fact in regard to alcohol and the blood pressure is that alcohol notably, consistently, and persistently elevates blood pressure after paralysis of the vasomotor system by high-up spinal section. This elevation of the blood pressure cannot be due to a local action upon the blood-vessel walls, otherwise it would manifest itself before section of the spinal cord, because any local action would necessarily show itself as much before as after removal of the dominant vasomotor nerve control. It appears to us that the effects of alcohol upon the blood pressure before and after section of the cervical cord are, when taken together in themselves, sufficient to show that alcohol consentaneously stimulates the heart and depresses the vasomotor centres. This conclusion is very strongly corroborated by the effect of alcohol in increasing the rate of the blood flow in the arteries. The blood flow may be increased by augmenting the force of the propelling power, or by diminishing the power of the resistance, or it may be enormously increased by simultaneously increasing the propelling power and decreasing the resistance. We have demonstrated that the rate of the blood flow is almost doubled by alcohol; indeed, the amount of this increase is so great as in itself to suggest that there must be a double factor in its production. Moreover, if an increase of the blood flow produced by the drug were simply due to cardiac stimulation, such cardiac stimulation would of necessity clearly register itself in the uninjured animal by a rise of the blood pressure, and this alcohol does not do; further, if the increased blood flow were solely the outcome of vascular depression, of necessity alcohol should in the uninjured animal produce fall of the blood pressure.

These three facts taken together, namely, lack of power to consistently increase or decrease blood pressure in the uninjured animal, possession of power to increase blood pressure after centric vasomotor paralysis, and possession of power to enormously augment the rate of the blood flow, lead to one inevitable conclusion, namely, that a drug which possesses these things must simultaneously stimulate the heart and widen the blood paths by depressing the vasomotor centres. Such, then, must be the action of alcohol.

The correctness of this conclusion is further corroborated by the results of our study of the action of alcohol upon the

[1] New York Medical Journal, xl., 1891.

isolated reptilian heart. It would apparently have been in order to have made studies upon the mammalian heart, but we have long since believed, as the result of careful study of the experimental methods and results heretofore published, that such experimentation is so surrounded with practical difficulties that the results reached are more apt to be misleading than true guides. The delicacy of the organ, the violence done to its natural conditions, the unexplainable results which have been reached by various experimenters, seem to us to show that until the technique of the method is radically improved little can really be learned from such experiments —possibly unless in the case of a drug like digitalis, whose cardiac action is overwhelming.

On the other hand, the power of the reptilian heart under favorable circumstances to continue at ordinary temperatures its functions for many hours, regularly and without pronounced abatement, evinces a lack of sensibility and a robustness of resistance to unnatural conditions which are the basis of successful experimentation. Moreover, all our physiological and pharmacological data show that so far as quality drug action is concerned there is no difference between the mammalian and reptilian heart. We can therefore confidently add to the facts previously summarized the further fact that there is direct proof that alcohol increases the heart work. In conclusion, *alcohol does not seriously affect the normal animal blood pressure, elevates the blood pressure after vasomotor paralysis from section of the cervical cord, increases the rate of the blood flow, and directly stimulates the heart; therefore, the general action upon the circulation of the moderate dose of alcohol is cardiac stimulation with vascular dilatation due to depression of the vasomotor centres.*

The conclusion reached in the preceding paragraph rests, as does the most of our knowledge in regard to the physiological action of drugs, upon experiments made upon the lower animals ; but it has occurred to us that these results might with a certain measure of plausibility be tested by plethysmographic studies upon human beings. Some experience with the plethysmograph has led us to believe that with this instrument incorrect results can very readily be reached, and that too much reliance can readily be placed upon its indications. When the arm is used, as is ordinarily done, insensible movements backward or forward have an enormous influence upon the lever which records the movements of the contained fluid. We have made two experiments with the arm plethysmograph, using every precaution to avoid fallacies and employing a person unaccustomed to the use of alcohol. In the first of these experiments whiskey was taken, in the second Mumm's extra dry champagne. In examining the results of these experiments it must be remembered that although it is theoretically possible to construct a plethysmograph the movements of the lever of which shall have an absolute value—in other words, represent the percentage of enlargement of the arm—such instrument must be made with great care and at much expense.

The University of Pennsylvania Laboratory does not own such an instrument, and our present purposes have not required it; all that we have attempted to do is to show whether there is or is not a distinct increase in the size of the arm following the ingestion of alcohol.

In the following tables, when the needle was above the norm, the amount above the norm is given in millimetres preceded by a +; when the needle was below the norm the descent is given in millimetres with a —. As already stated, these millimetres are no absolute measure of the amount of expansion and contraction of the volume of the arm.

Table I.

Minutes.	Plethysmographic lever.
0 whiskey 50 c.c.	Norm.
20	Norm.
30	+ 13 mm.
40	+ 15 mm.
60	+ 7 mm.
80	+ 5 mm.
90	— 1 mm.

Table II.

Minutes.	Plethysmographic lever.
0 champagne 198 c.c.	Norm.
7	+ 24 mm.
11	+ 13 mm.
14 champagne 198 c.c.	— 10 mm.
15	+ 27 mm.
19	+ 22 mm.
27	+ 27 mm.
30	+ 7 mm.
34	— 11 mm.

The above records are entirely concordant with one another, differing only in the fact which is constantly indicated in human life, that distilled liquors like whiskey act more slowly and persistently than does champagne. In each experiment under the influence of alcohol there was a distinct increase in the size of the arm; with the whiskey slowly and gradually, with champagne rapidly developed ; and with whiskey much more permanently maintained than with champagne, the rise after a time being followed by a slight decrease in the size of the arm below normal.

The increase in the size of the arm in these experiments is not readily explainable except with the supposition of increased amount of blood in the organ due to dilatation of the bloodvessels. The results, therefore, are entirely concordant and corroborative with those reached by experiments upon animals.

The conclusions reached in the present research throw much light upon the practical problem of the therapeutical effects and uses of alcohol, indicating that some results which have been supposed to be due to a direct action of the drug are probably secondarily produced by the increase of the activity of the circulation. A scientific journal like the present is hardly the place for a discussion of problems of practical medicine, but it may be allowable to point out how this new knowledge relates itself to the action of the drug upon the cerebrum. There is, on the one hand, at present no sufficient proof that alcohol is a direct cerebral stimulant such

as is caffeine; unless it be in exceptional cases of exhaustion or narcotic habit, it is doubtful whether it directly augments the working power of the brain. Again, so far as consciousness is concerned, its tendencies are to produce sleep rather than wakefulness, while the true cerebral stimulant, augmenting the functional activity of the cortical centres, lessens their tendency to go into a condition of functional rest, *i. e.*, sleep. On the other hand, any *habitue* of feasts where wines circulate freely knows fully well the increase of amount and brilliancy of conversation which occurs *pari passu* with the flushing of the cheeks. It is probable that this cerebral excitement and increased activity are due not to the direct action of the drug upon the brain, but to the enormously increased flow of blood running riot through the brain.

NOTE ON THE OCCURRENCE OF EPIDEMIC CEREBROSPINAL MENINGITIS IN PHILADELPHIA, WINTER 1904-1905.

By A. C. Abbott, M.D.,

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Within the past few months attention has been directed to the question of epidemic cerebrospinal meningitis, because of its more or less alarming prevalence in a number of localities in this country and abroad.

The occurrence of a larger number of cases of this disease in Philadelphia than is usually seen has given rise to much apprehension, and fear is expressed that the malady may develop to epidemic proportions. Since the disease has been generally regarded as transmissible from person to person, and is, in Pennsylvania, included among the contagious diseases provided for by Act of Assembly of 1895, it is appropriate at this time to make a brief statement of the conditions in Philadelphia that have been officially recorded during the past fall and winter, and the present spring.

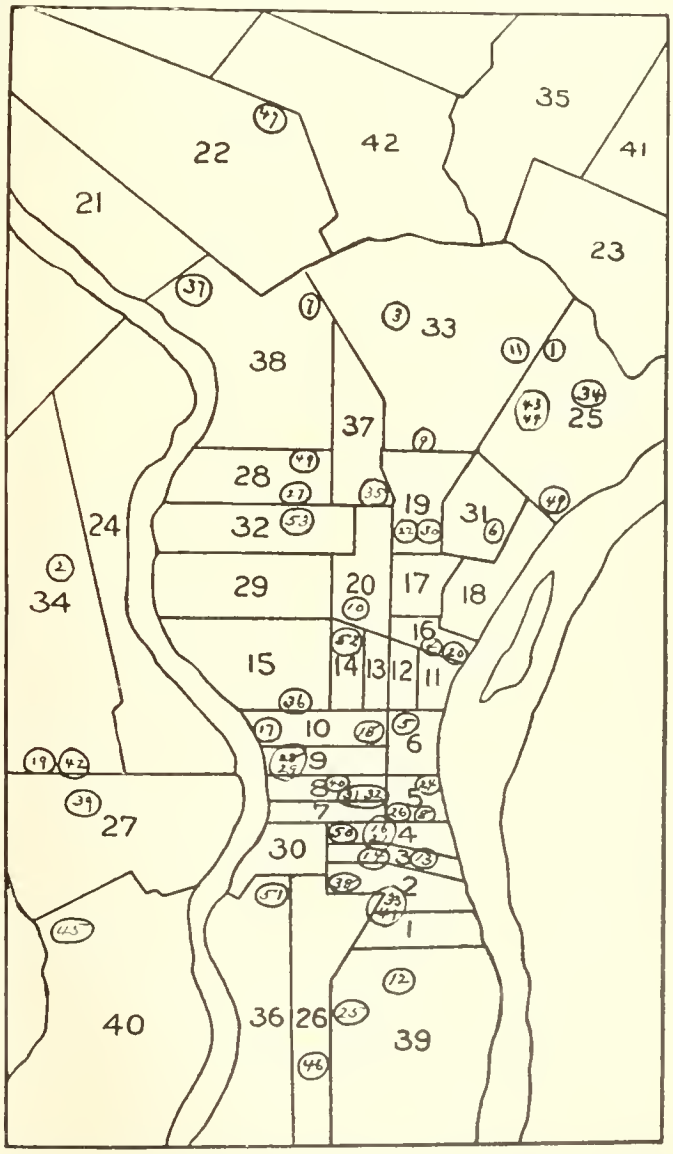
Prior to September of 1904 there was little or no insistence that cases of the disease be reported during life; in consequence, for a series of years preceding that date, it is common to find occasional deaths recorded, without any record of the cases prior to death. While it is, therefore, impossible to speak of the number of cases existing in preceding years, there is no doubt, from the mortality lists, that a certain number of these cases are always present in large communities.

Beginning with September of 1904, the month in which the cases began to be regularly reported to the Bureau of Health, we find between that date and April 7th (the date of writing) that 52 cases of epidemic cerebrospinal meningitis, with 17 deaths, have been recorded.

Useful clinical histories of 32 of these cases have been secured, and a perusal of this group shows that 5 of the cases were true tuberculous meningitis; 2 were proven at autopsy or by lumbar puncture to be due to pneumococcus infection; while the histories of 6 make it impossible to classify them as of the genuine epidemic type of meningitis.

Without making a correction for doubtful cases, the death rate up to the present has been 30.7 per cent.

Of all cases recorded 3.6 per cent. occurred among children under one year of age, 70.9 per cent. among those between



Showing approximate location and order of occurrence (numerals enclosed in circle) of cases of cerebro-spinal meningitis in Philadelphia between September, 1904, and April 7, 1905.

one and twenty years of age, and 25.5 per cent. among those over twenty years of age. No case was reported in a person more than forty-five years of age.

The order in which the cases occurred reveals no deviation from the course of epidemics as seen in other localities, and offers little to support the opinion that the epidemic development of cerebrospinal meningitis depends upon the direct transmission of contagion from one person to another.

In the accompanying chart of the city, the figures show both the succession of cases and the approximate location of each case. From this chart it will be observed that the first recorded case is in the Twenty-fifth Ward, while the second is miles away in the Thirty-fourth Ward, the third being in the Thirty-eighth Ward, and so on.

In September, 1904, 1 case was reported; in November, 2; in December, 5; in January, 1905, 2; in February, 13; in March, 22, in April, up to 7th, 8 cases were reported.

The largest number of cases reported on a single day was 5 (February 20th), while 4 cases were reported on April 6th.

In only four instances have more than one case been reported from a single house. In each instance there were 2 cases to a house. In two of the houses the cases developed simultaneously; in the third house there was an interval of three days, and in the fourth an interval of six days between the development of the cases.

In the last two houses there is a possibility of there having been a direct transmission from person to person; these, together with the experience of our lamented brother practitioner, Dr. Craig, are the only instances seen that suggest the possible direct transmission of the contagion.

Notwithstanding the scarcity of evidence of its transmissibility, the disease is being treated as contagious—*i. e.*, the houses containing cases are placarded; the cases are isolated in so far as is possible; where circumstances demand it, their removal to the Municipal Hospital is advised, and all premises occupied by the patients are disinfected.

The epidemiological factors that underlie the widespread development of this disease are not known. The majority of outbreaks have occurred in winter and in spring, and also at wet and rainy times, though the disease has been known to arise and continue in summer and in dry seasons.

A number of investigations point to causative conditions, probably analogous to those concerned in the widespread development of pneumonia. Just as the germ of pneumonia is found in normal human beings and in disease conditions other than pneumonia, so the epidemic germ of meningitis, and the other germs that have been found in connection with the disease, are seen in normal persons and in convalescents from other maladies.

It is possible, maybe probable, that some undetermined factor favors the frequent autoinfection among well persons who may be harboring the germ of the disease.

Several conditions, especially overcrowding, are generally regarded as important predisposing factors, and in many recorded outbreaks there seems to be justification for this view, but in a few it is contradicted. For instance, in the outbreak in Boston during the winter of 1897 and 1898, cases of the disease were as frequent among the well-to-do as among the poor of the crowded districts.

Physical and mental exhaustion, as well as exposure to extremes of weather, prepare the body for this type of infection, just as they do for most other infective diseases. At the present time the disease has certainly not reached epidemic or alarming proportions in this city. Its future course and development cannot, manifestly, be predicted.

CONCERNING METASTATIC OPHTHALMITIS, WITH THE REPORT OF A CASE OF THIS AFFECTION WHICH DEVELOPED THIRTY-ONE DAYS AFTER CONFINEMENT.

By G. E. de Schweinitz, M.D.,
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Although many cases of metastatic ophthalmitis have been recorded, each new one is surrounded with certain features of interest which render its description useful.

Mrs. H. B., aged thirty-eight, came to the Dispensary for Diseases of the Eye in the University Hospital, February 12, 1904, on the recommendation of her physician, Dr. O. D. Schaul, to whom I am indebted for the history which follows:

History. The patient, a multipara, fell in labor at six o'clock on the morning of December 19, 1903; it terminated at twelve o'clock on the same day, the child presenting in the first position, and delivery being accomplished without accident or complication. There were no visible tears in the cervix or perineum. During the following eight days the patient's condition was perfectly satisfactory, the pulse and temperature being normal and the lochia moderate in amount and of natural quality.

On January 1st, or twelve days after her confinement, the patient went into the basement kitchen of her house and prepared breakfast. A few hours later a sudden violent uterine hemorrhage occurred, which stopped abruptly after the first gush was over, and was not repeated. It is estimated that about one quart of blood was lost. For the next eight days the woman was carefully watched and nursed

and no untoward symptoms appeared. On the ninth day severe pain began in the left gluteal region, which later extended along the sciatic nerve of the same side; there was also pain in the hips, knees, shoulders, and wrists. These phenomena were accompanied by fever and headache, but an initial chill was not noted. Amelioration of these symptoms took place during the following nine days, and the patient was seemingly making a satisfactory convalescence, when, on January 19th, or thirty-one days after confinemet, and ten days after the joint involvements, pain in and around the right eye developed. Vision was not lost, only much blurred, and examination by Dr. Schaul revealed some haziness of the cornea and a few grayish deposits on the iris and on the capsule of the lens. Ophthalmoscopic examination was not attempted. The ocular complications grew rapidly worse, and four days later the appearances were those of panophthalmitis, with protrusion of the globe and great œdema of the lids. The patient's temperature at the time was 104°. Twelve days after the ocular inflammation began a rupture of the lower sclera occurred, with the escape of some purulent fluid. The patient continued under treatment in her own home until February 12th, when she was admitted to my wards in the University Hospital.

Examination. The patient, a sallow-faced woman of the brunette type, with pallid lips, exhibited the facial characteristics of one who had suffered much pain. The temperature on admission was 99.2°, the pulse 112, and the respirations 26. She voided thirty-one ounces of urine during the first twenty-four hours, which presented the following characteristics: Color, amber and cloudy; reaction, acid; specific gravity, 1020; albumin, a distinct reaction; sugar, none; sediment, mucopurulent, which contained pus and bladder and vaginal epithelium, but no casts.

Physical examination failed to reveal the presence of cardiac or pulmonary lesions. There was no tenderness on abdominal palpation and no redness or apparent involvement of any joints. The blood examination was as follows: Red blood corpuscles, 4,640,000; white blood corpuscles, 15,120; therefore a slight leukocytosis.

Eyes. O. D. V. = no light perception. The lids were swollen and slightly brawny. There was intense chemosis of the bulbar conjunctiva and swelling of the tarsal portion of this membrane. The cornea was clear, the iris swollen and discolored, and behind the pupil the well-known yellowish reflex, giving rise to the appearance ordinarily known as pseudoglioma. Below the inferior border of the cornea there was an irregular rupture of the sclera covered with swollen conjunctiva.

O. S. Uncorrected vision 6/9, with + 2.50. V. = 8/7.5. The eyeground was normal and there were no lesions in the media and fundus nor on the surface of the globe.

At my request Dr. John G. Clark made an examination of the patient and reported as follows: "I have examined Mrs. B. and find no evidence of residual puerperal infection. The pelvic floor is intact, the uterus is in normal anteflexion, freely movable, and not tender on even deep pressure. The ovaries and tubes are normal."

The patient was placed upon tonic and supporting treatment; the eye frequently irrigated with a saturated boric acid lotion, and a 25 per cent. solution of argyrol instilled into the conjunctival sac at suitable intervals. Six days later, the temperature having dropped to the normal point, the right eyeball was enucleated with some difficulty, as adhesions had formed between it and the surrounding tissue. Convalescence was uneventful and at the end of a week the patient was discharged with a normal socket and entirely free from pain and discomfort.

The enucleated ball was hardened in formalin, divided in the usual manner, one-half being mounted in glycerin jelly and the other half submitted to microscopic examination.

Bacteriological examination of the purulent material in the interior of the globe yielded the following results: Gram positive; micrococci both intracellular and extracellular, probably staphylococci; streptococci occurring in chains; a few bacilli, resembling the bacilli diphtheriæ were found, but their exact nature was not positively determined.

Macroscopic Examination. The divided eyeball measures 24 mm. in its vertical and 22 mm. in its horizontal diameter. The cornea is intact, there is a yellowish-red exudate in the anterior chamber, and the thickened iris is firmly in contact with the surface of the lens. The lens itself is swollen and elongated backward and presents a somewhat conical shape. The ciliary bodies are detached and drawn toward the lens by a contracting exudate, leaving in the upper portion a cyst-like space between the detached ciliary body and the overlying sclera, which at this point is considerably thinned. Just posterior to the ciliary region in the lower half of the eyeball there is a rupture through the sclera 5 mm. in width, which is filled with a purulent exudate. The entire interior of the eyeball is filled with a yellowish-red, purulent-looking material, especially massed just posterior to the lens, where the color is more nearly yellow than the remaining portions, which are red and yellow mixed. The sclera is markedly thickened and infiltrated, and its wall in many places 3 to 3.5 mm. in thickness, while that portion which overlies the cyst-like cavity between the detached ciliary body and the scleral covering is not more than $\frac{1}{2}$ to $\frac{3}{4}$ mm. in thickness.

The cornea is intact and shows no pathological changes, either in its epithelial covering, its main structure, or its endothelium. Just below the corneoscleral junction the conjunctival epithelium is elevated and beneath it is a purulent collection through which pass some of the wide-mouthed bloodvessels. The lens is swollen, its posterior capsule is eroded, and its cortex cataractous. The iris is thickened and well infiltrated with small round cells. It is firmly attached to the capsule of the lens. The ciliary bodies are

densely infiltrated with mononuclear cells and are detached from the sclera. The space between the detachment of the ciliary bodies and the sclera is filled with an albuminous exudate, a similar exudate being visible in the anterior chamber. The choroid is enormously thickened, and its proper structure can scarcely be recognized owing to the substitution of its elements by the mononuclear cellular exudate. In the regions toward the sclera the pigment cells of the stroma proper can be seen. The retina is nowhere to be recognized, its structure having been entirely destroyed. Owing to the fact that the optic nerve was cut very close to the sclera, a section of it does not appear in the specimens thus far examined. The entire vitreous is converted into a purulent mass, the cells being polymorphonuclear and many of them in a high state of degeneration. The greatly thickened sclera is everywhere infiltrated with round cells, this infiltration being especially marked in its inner strata. Through its ruptured wall in the inferior portion the same character of purulent exudate which fills the interior of the eyeball is seen escaping. On the surface of the vitreous exudate in properly stained sections chains of streptococci are visible.

Remarks. Since the publication of Axenfeld's[1] well-known dissertation on purulent metastatic ophthalmitis, systematic writers have been accustomed to classify this affection from the etiological standpoint into four groups, viz., metastatic ophthalmitis, which results from (*a*) puerperal pyæmia, (*b*) surgical pyæmia, (*c*) cryptogenetic septicopyæmia, and (*d*) infectious diseases.

Puerperal pyæmia is the most frequent cause of metastatic ophthalmitis, and the ocular complications may be unilateral or bilateral. According to Axenfeld, the mortality in the bilateral cases is 85 per cent., which Groenouw thinks is too low, and in the unilateral cases 21 per cent. Ulcerative endocarditis is a frequent complicating factor. The ophthalmitis develops usually during the first two weeks of the disease, but may be detained until the seventh week. In so far as life is concerned, it apparently makes no difference whether the eye conditions appear early or late.

According to Groenouw[2] surgical pyæmia should include all cases which arise from injuries, operations, and local purulent areas, even when the last-named conditions are non-traumatic, but have an internal origin and have their situation in the mucous membrane of the digestive, pulmonary, and urinary organs. With these he would also include all infections of non-puerperal origin which proceed from the sexual organs. Metastatic ophthalmitis arising from such causes may also be unilateral or bilateral, and may appear as early as the first day of the disease and as late as the forty-fifth day. Naturally, the bilateral cases present the gravest prognosis and yield a mortality of not less than 75 per cent.

By cryptogenetic pyæmia is meant a condition in which the point of entrance of the infection has not certainly been determined and which gives rise to septic manifestations which may appear in the guise of an infectious disease, or simply of a general *malaise* associated with fever. The microbes gain entrance through the mucous membranes without causing in them definite alterations. Axenfeld, whose description has just been quoted, includes in this class cases of so-called "catching cold," of ulcerated endocarditis, and cases which manifest themselves with the clinical symptoms of joint rheumatism, or are analogous in their course to typhus, meningitis, and miliary tuberculosis, and, finally, those cases of undetermined general febrile disturbance from which endogenous infection of the eye arises. Under conditions like these the ophthalmitis, either unilateral or bilateral, may proceed to panophthalmitis, or occasionally to phthisis bulbi without preceding purulent choroiditis. The ocular lesion may be, although rarely, the only discovered metastasis during the disease.

Finally, a certain number of cases of metastatic ophthalmitis arise from various infectious diseases, particularly pneumonia, influenza, measles, scarlet fever, diphtheria, variola, etc.

The interesting point to determine in the present instance is with which one of the four groups it should be classified, for in some respects the clinical features are in accord with each of them. It surely may be stated that this ophthalmitis was not the result of any active puerperal infection in the ordinary sense of that term, for twelve days after labor the woman was in perfectly good condition, and then, following imprudent exposure, had a sharp uterine hemorrhage, but no florid symptoms until the ninth day after its occurrence, when the joint pains, headache, and rise of temperature developed. These are very well explained by a mild sepsis, and probably mean that some nidus of infection in the uterine wall or mucous membrane gave rise to metastasis, not sufficiently severe in the joints to produce permanent lesions, but sufficiently great in the eye to cause the ophthalmitis which has been described. It is curious, however, that so skilful an examination as that made by Dr. Clark failed to reveal any signs of uterine involvement thirty-one days after labor. Indeed, in his letter to me, already quoted, he states that ordinarily he would doubt if the uterus should be made responsible for the purulent condition of the eye had he not seen on post-mortem a small area of purulent infiltration in the uterine wall crowded with streptococci, which was not evident to clinical exploration, but found only after serial sections of this organ were made. Therefore, the mere absence of symptoms on digital examination would not exclude the possibility of such a lesion. In a certain sense this case could be described as a

[1] Archiv f. Ophthal., Band xl., Heft 3, pp. 1–129, and Heft 4, pp. 130–198, 1894.

[2] Graefe-Saemisch, Handbuch der Gesamten Augenheilk., 1904, 10, 504.

cryptogenetic variety of ophthalmitis, and that the exposure to which the patient submitted herself on the twelfth day after labor caused her in vague terms to "catch cold," and that the joint involvement should be regarded as analogous to that which occurs in ordinary rheumatism, the entry port of infection being the mucous membrane of the uterus, which failed to reveal itself by any permanent alterations. Again, it might be classified as a surgical pyæmic ophthalmitis, with the idea that some local area in the uterine wall, pus-bearing and infected, as has already been suggested, was the nidus from which the micro-organisms proceeded, and which would have been discovered only in post-mortem section. Taking into consideration the uterine hemorrhage on the twelfth day after confinement, the succeeding joint complications associated with febrile manifestations and followed by the ophthalmitis, it would seem the case should be regarded as one due to a puerperal infection of tardy devlopment and minor severity, with its chief metastasis in the eye.

In conclusion, a word may be said, in general terms, as to the pathogenesis of metastatic ophthalmitis. Numerous investigations indicate that it arises by virtue of the entrance of septic masses into the capillaries of the eye, and according to Axenfeld's researches in double-sided ophthalmitis, the retina is exclusively, or at least almost always, first affected, but in one-sided varieties the uveal tract is also involved. Evidently the infected masses are so small that they are able to pass freely and enter the narrowed capillaries of the retina. The visual disturbances which follow rapidly are due essentially not to the emboli, but to the widespread septic inflammation which they create.

Concerning the bacteriology of this condition in the puerperal cases it may be said that streptococci have almost always been found, and in the surgical varieties staphylococci. Some forms of ophthalmitis have been caused by the Fraenkel-Weichselbaum pneumococcus, and when this has been the microbe concerned most frequently those cases have been observed in which phthisis bulbi has resulted without preceding panophthalmitis. In the present instance there seems to have been a mixed infection, inasmuch as both staphylococci and streptococci were present. The bacilli found were not identified.

A STUDY OF FIFTY CASES OF PERFORATION IN TYPHOID FEVER.[1]

By J. Alison Scott, M.D.,

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The results of this study of perforation in typhoid fever are based upon a series of cases occurring in the wards of the Pennsylvania Hospital from 1901 to the present date. They include not only the cases under my own personal care, but also all those that have occurred in the wards of my medical and surgical colleagues at the hospital, to whom I am indebted for the privilege of their study. I have included in the table of perforative cases all those abdominal conditions occurring in typhoid fever and caused by that infection of sufficient gravity to bring the case to operation. Thus, there will be found in the table one case of ruptured mesenteric gland and several cases of appendicitis, the latter, however, due to the presence of typhoid ulceration within the appendix and not a simple inflammatory change, such as is common in ordinary appendicitis. I have, on the contrary, thrown out of the perforative cases those of appendicitis occurring during the course of or as a sequel to typhoid, and cases which though considered as perforative were not so demonstrated either at operation or at autopsy. In the study, therefore, of the perforative cases the perforation was discovered either at operation or at autopsy.

[1] Read before the Section on Medicine of the College of Physicians, January 9, 1905.

CASES OCCURRING IN THE PENNSYLVANIA HOSPITAL SINCE MAY, 1901.

Year.	No. of cases.	Total deaths.	Perf.	Operations.	No oper	Recov.	Per cent. (recov.)
May, 1901-1902	509	35	8	5	3	.	
May, 1902-1903	749	55	17	13	4	6	16.1
May, 1903-1904	690	63	24	19	5	6	30.1
May, 1904 *et seq.*			7	6	1	.	
	1948	153	56	43	13	12	29.5

From the above figures it is easily seen that in 1948 cases of typhoid there occurred 153 deaths, a total mortality of 7.8 per cent. Of this same number of cases there occurred 50 cases of perforation, for 1 case is not included in this table of statistics, no reference to it being obtainable. The perforative percentage is therefore 2.6. Unfortunately, neither the number of cases nor the mortality for the present year can be obtained, so that the 7 cases which have occurred since May, 1904, cannot well be included in the above figures.

THE FREQUENCY OF PERFORATION CALCULATED FROM STATISTICS IN VARIOUS HOSPITALS.

The following figures regarding the frequency of perforation in the English hospitals I have taken from an

article by Hector Mackenzie (*Lancet*, September 26, 1903). It includes the cases during a series in four of the London hospitals: St. Bartholomew's, St. Thomas', Middlesex, and Charing Cross. They total:

Hospital.	No. of cases	No. of deaths.	Perforations.
St. Bartholomew's, St. Thomas', Middlesex, Charing Cross	2533	340	117
Brisbane, Royal Victoria, Johns Hopkins	3351	240	90
Eastern (Goodall, *Lancet*, July 2, 1904, ten year series)	1921	304	96
Pennsylvania (since May, 1901), Philadelphia	1948	153	48
	9753	1037	351
Mt. Sinai Hospital, New York, 1902 to 1903 (Morris Manges)	216	..	19

These figures show that one death out of every 3 is due to perforation, which is a larger percentage than is usually supposed; 1 death in every 4 has been considered a large estimate. In 1902, 9 cases, 1 recovery; in 1903, 10 cases, 4 recoveries, 8 per cent.

In European countries the frequency of perforation is certainly much less than in either England, Canada, Australia, or America. The statistics of Hölscher (Munich, 2000 autopsies, 114 perforations, 5.7 per cent.), Leibermeister (Basle, 2000 autopsies, 26 perforations, 1.3 per cent.), and Schultz (Hamburg, 3686 autopsies, 44 perforations, 1.2 per cent.) show that perforation is unquestionably much commoner in our cases.

TYPHOID STATISTICS IN THE UNITED STATES FOR 1900.

In connection with what has been said before in regard to the proportion of perforative cases among the fatal cases, the statistics of the whole country are somewhat interesting.

I find in 1900 that typhoid fever occupies the fourth place in the mortality list. Consumption, "the white plague," heads the list by claiming 109,750 victims; it is closely followed by pneumonia, "the captain of the men of death," with 105,971 deaths; while heart disease accounted for 67,439 deaths. Typhoid fever caused in the same year 35,379 deaths. If this view is correct that 1 death in every 4 is due to perforation, among these fatal cases were 8841 perforations and operations estimating the mortality at 75 per cent. might have yielded 2211 recoveries. It is interesting and at the same time mortifying to have to acknowledge that Pennsylvania heads the entire list of States and Territories in its number of deaths from typhoid—2779. It is followed by Texas, a State of eight or ten times our area, with 2041 deaths. Illinois, Ohio, and New York follow with 1897, 1795, and 1776 deaths respectively.

Assuming, therefore, that 1 death out of every 4 is due to perforation, 8881 perforative cases occurred throughout the entire country in 1900. Assuming that the mortality of all the operative cases is at least 75 per cent., operation in all these cases might have resulted in the recovery of 2211. These are large figures and mean many important lives. In Pennsylvania alone the total number of lives saved would have numbered about 232.

THE STUDY OF THE FIFTY PENNSYLVANIA HOSPITAL CASES.

AGE.

5 to 15 years	7 cases.
15 " 25 "	15 "
25 " 35 "	16 "
35 " 45 "	8 "
45 " 55 "	4 "
Total	50 "

It will be noticed that the greater majority of these cases occur in patients under thirty-five years of age, that is 36 of them did so. This of course is but to be expected, as typhoid fever is a disease of the young. The youngest case was eight years of age and the oldest was a man of fifty-two years. But 4 of the cases are over forty-five years of age, and in each of these, as reference to the abstract of cases will show, some difficulties were presented in the diagnosis of typhoid fever, and in 2 (Cases XXII. and XXXII.) neither typhoid nor perforation were suspected.

SEX. Forty-five cases occurred in men and boys, and 5 in women.

COLOR. Forty-three were white, while 7 were negroes.

DATE OF PERFORATION—DAY OR WEEK.

First week	2
Second week	10
Third week	22
Fourth week	7
Fifth week	7—36
Sixth week	1
Seventh week	1

Forty-six of the cases occurred between the second and the fifth week inclusive—92 per cent.

Some comment on the date of perforation is perhaps essential. Among these cases were 2 which occurred in the first week, 1 on the second and 1 on the sixth day. On careful inquiry, however, into the history of these cases it is discovered that the boy who perforated on the second day of his illness was in reality a perforation in a relapse; as we get the history of his having been sick in some hospital for three or four weeks, a month prior to the time of perforation. It is difficult, however, in this case to establish the fact that he had fever or other evidences of relapse. The other patient had been ill six days before admission to the hospital and there is no history of a previous illness in this case. In fact the man was seized while at work with severe abdominal pain, and when admitted to the hospital was almost in *articulo mortis*. This therefore seems to be

a case of perforation out of a clear sky. The latest date of perforation in this series of cases is the forty-sixth day. This man had an intercurrent relapse beginning on the twenty-seventh and lasting until the fortieth day, with perforation after convalescence was about established.

Severity of Cases. Six cases were mild (Nos. 14, 32, 36, 41, 46, 47); 10 cases of ordinary type (Nos. 5, 11, 12, 19, 22, 23, 28, 30, 35, 43); 27 were severe, and in 7 no previous history was recorded, though in several of them the symptoms were mild.

Analysis. Six of the 50 cases in which perforation occurred are classified as mild. There was but slight fever, few or no nervous symptoms, while the duration of the disease was short. Ten of the cases are considered as ordinary moderate fever of mild nocturnal delirium, no unusual evidences of severe infection. Twenty-seven of the cases are considered as severe, the disease being associated with low delirium or rapid pulse, chills, high temperature, secondary pneumonia, or hemorrhage, etc. In 7 cases there is no previous history.

Conclusion. Perforation occurs in the severe cases in more than one-half of their number. One-third of the cases in which perforation occurred can be classified as ordinary or mild attacks. In some few instances perforation occurs out of a clear sky (Nos. 8 and 33); neither of these men were supposed to be ill at all at the time of the onset of symptoms due to perforation.

Relation of Perforation to the Ileocæcal Valve. Within twelve inches, 19 cases; within twelve to twenty-four inches, 6 cases; within twenty-four to thirty-six inches, no cases; within thirty-six to forty-eight inches, 4 cases. In the ileum but the exact position not stated, 14 cases. In appendix only, 4 cases; in transverse colon and cæcum, 1 each; and 1 perforating mesenteric gland.

Analysis. In 43 of the total number of cases, or 86 per cent., the ileum was the seat of perforation. In 19 of the cases the perforation was in the first twelve inches above the ileocæcal valve, and of this number full 60 per cent. about 20 to 25 cm. (8 or 10 inches) above the valve. In the second twelve inches above the valve were found 6 cases of perforation; in the third foot above the valve no perforations were present, while there were 4 in the fourth twelve inches of the gut. In 14 cases no record of the exact situation is to be found, though the perforation is in each history explicitly stated as "in the ileum." In 3 cases not only were there perforations present in the ileum, but in Cases VII. and VIII. the appendix was perforated as well, and in Case XLVI. the cæcum. In 4 cases the appendix only was perforated (Nos. 11, 22, 26, 47). In 1 case the posterior surface of the transverse colon was perforated (No. 16); the cæcum only in 1 case (No. 29); while in Case XLIII. there were necrosis and rupture of the ileocolic mesenteric gland.

Conclusion. The greater majority of perforations of the bowel occur within twelve inches of the ileocæcal valve. In this study the greatest distance above the ileocæcal valve of perforation was 115 cm., forty-six inches (Case XXXIX.).

In Mackenzie's collection of 264 cases the jejunum was perforated twice, the ileum 232 times, the large intestine 22, and the appendix 9 times.

Size of Perforation. In this study classification as to the size is difficult. In the haste of operation there is no time for measurements to be taken, and as the gut is sutured in all cases of operation the size of perforation can only be approximated even at autopsy. The comparisons in the notes are usually made to some well-known object, such as pin-heads, lead-pencils, etc., and this classification will be subsequently used. Two distinct varieties of perforation are, however, seen; the one is usually single, small, circular in form, pin-point in size, and due to the extension of a necrotic process through the base of a small ulcer, frequently involving only a limited portion of it. This is much the commoner variety. A second variety is produced by a distinct area of gangrene or focal tissue necrosis involving a considerable area of the gut and at times suddenly dropping out *in toto*. It ranges in size from that of the finger-tip to a fifty-cent silver piece. At times one or more minute perforations may be found in such an area of necrotic gut. Such perforations are ragged holes of greater or less extent, permitting the rapid and free escape of the intestinal contents into the peritoneal cavity. The symptoms in the two varieties are sometimes widely different, though mistakes may be made as to their proper interpretation. In the 50 cases analyzed the perforations were pin-head in size in 14; slate-pencil in 3; lead-pencil in 4; ten-cent piece in 3; fifty-cent piece in 1. Two perforations were in the appendix; in 23 cases no special size of perforation is mentioned, though under such circumstances the perforation was usually small. In one or two of the cases the perforations were small slits in the intestine along its long axis, with one or more small pin-point perforations at either extremity.

Number of Perforations. In 42 cases but a single perforation was present; in 2 cases, 2; in 2 cases, 3; in 1 case, 4, and in one case 6; in 2 cases no mention is made of the number.

Important local Symptoms. I consider the three most important local symptoms of perforation of the bowel to be (1) pain, (2) tenderness, (3) rigidity.

Pain. Sudden, sharp, and severe pain in the abdomen is present at some one time in the majority of cases, yet not in all. As has been shown by other observers (McCrae), abdominal pain is present in a very considerable proportion of all cases of typhoid. An analysis of our 50 cases results as follows: sharp, sudden, severe localized pain was present in 25 cases; pain of sudden onset becoming general in 3 cases; pain of slow onset with general localization in 9 cases. No pain was complained of in 6 cases; there is no mention of any pain in 3 cases; while in 4 cases there is no previous history of the symptoms present at perforation, operation

being performed immediately after admission to the hospital. The analysis of the above figures, therefore, shows that in 50 per cent. of the cases the onset of pain was sudden, sharp, and severe with definite localization to some one abdominal zone or zones. In 18 per cent. the onset of the pain was gradual, but increasing and over the whole abdomen. In 6 per cent. the pain was of sudden onset, but generalized over entire abdomen. In 12 per cent. there was no pain at all complained of or noticed. In 8 per cent. no good history could be secured, all of the 4 cases presenting signs of general peritonitis. In 3 cases there is no mention of pain, though the abdomen was tender on palpation.

Conclusions. Pain of some kind is present in 74 per cent. of all the cases. In half the cases the pain is sudden, severe, and agonizing, causing the patient to cry out or wakening one from a sound sleep and localizing itself to a special zone. In one-fifth of the cases the pain is of slow onset, in no special zones, but general. In 12 per cent. of the cases there was no pain. These are the cases that usually escape observation and are undiagnosed.

Localization of Pain. In 9 cases the pain was localized in the right iliac region; in 12 cases to the right side, that is, to both upper and lower zones. This is a total, therefore, of 21 cases of right-sided pain. In 1 case pain was most severe in the left iliac region. In 2 cases it was most severe on the left side. In 3 cases both lower zones were mainly affected. In 1 pain was felt over the bladder, and in 13 cases was generalized over the entire abdomen. In 1 case the pain was primarily felt in the testicles and abdomen. In 4 cases there is no good previous history, while in 4 other cases there was no pain to be localized.

Pain at the Onset of Attack. I analyzed these 50 cases in regard to the presence of pain at the onset of typhoid. I find that 21 cases complained of abdominal pain more or less severe as one of their prominent symptoms (Nos. 2, 3, 4, 5, 7, 16, 17, 22, 26, 27, 29, 30, 31, 36, 37, 39, 40, 41, 42, 12, 17, 48). In 6 cases there was no mention of this symptom, and in 16 cases no pain was complained of. In 7 cases there was no previous history.

Analysis. In 21 cases, or 42 per cent., abdominal pain was complained of at the beginning of the attack and present on admission, often with some general tenderness. After twenty-four hours in bed with regulation of diet the pain commonly disappeared. In 16 cases there was no pain at the onset of the disease. In 6 cases there is no record of pain found in the history, and 37 cases are therefore available for study.

Conclusion. One-half of the perforative cases complain of abdominal pain early in the disease.

T. McCrae has studied 500 cases of typhoid with special reference to the presence of abdominal pain at times other than at the onset of the attack. Pain was present in 161 of these cases, or 32.2 per cent. In 13 it was due to perforation; in 13 to hemorrhage; while in 70 cases no discoverable cause could be ascertained.

Analysis of Site of Localization of Pain. In 9 cases, 18 per cent., the pain was definitely located to the right iliac region; in 12 cases, 24 per cent., the pain was on the right side, that is, both upper and lower zones; in but 1 case was the pain in the left iliac region, and in but 2 on the left side; in 3 cases, 6 per cent., the pain was localized to both lower abdominal zones.

Conclusions. In 42 per cent. of cases the localization of the pain is on the right side of the abdomen, while in 26 per cent. there is no special area complained of, the patient simply stating the stomach is painful. In not a few of these cases whether the pain be right-sided or left-sided it localizes itself about the umbilicus.

Tenderness. Tenderness was present in 37 cases; was absent in 3 cases; 7 cases were not under observation at the time of onset; and in 3 cases no mention is made of tenderness in the history. (Cases X., XII., XVI., XIX., XXXII., XXXVI., and L. are all of interest in this study, showing the absence of both tenderness and rigidity which occurred in 3 cases, Nos. 32, 36, 40, or tenderness being present with absence of rigidity in Cases XII., XVI., XIX.)

Rigidity. Muscle spasm or rigidity was present in 33 cases; in 6 it was absent; in 7 no previous history was obtainable, and in 4 no mention of this symptom is found. By the above analysis it is readily seen that tenderness is present in at least three-fourths of all the cases, and it has usually been at or near the localization of the pain complained of. It shows also that tenderness in the abdomen exists about as frequently as pain either sudden or slow is actually complained of (74 per cent.). The dull, stuporous conditions and the patient's inability to appreciate pain in cases of severe typhoid toxæmia must be taken into consideration here. Also the fact that the active hemorrhagic cases (see below) are frequently kept well under the influence of opium in some form and do not feel pain even if present to any great extent. In the 3 cases in which both tenderness and rigidity are absent the diagnosis failed (Cases XXXII., XXXV., L.); and in 1 case in which tenderness was absent but muscle rigidity present (No. 36) and a second case (No. 16) with much localized colonic tenderness and no rigidity, a proper diagnosis was not made.

From the above figures it can be seen that rigidity is absent in 12 per cent. of the cases, more frequently than is tenderness, 6 per cent. In the cases classified under no previous history I include those cases in which perforation occurred before admission to the hospital and which were therefore not under our observation at that time; on admission they all presented signs of either local or general peritonitis with tenderness and rigidity.

Conclusions. Tenderness on palpation is present in at least 75 per cent. of cases of perforation, while rigidity or muscle spasm is present in at least 66 per cent.

Additional Local Symptoms. *Condition of Abdomen; the Absence or Presence of Distention.* Distention was present in 24 cases; in 12 cases the abdomen was not distended; in 4 cases it was retracted; in 7 cases there was no previous history; while in 3 no record can be found of the condition present.

Analysis. In 24 cases the abdomen is noted as more or less distended; in a considerable proportion of these cases distention was already present and increased subsequent to symptoms of perforation. In not a few of the cases included, distention is noted as coming on some six to eight hours after suspicious symptoms. In very few cases was it immediately noted, yet in 48 per cent. of the cases the abdomen is recorded as "somewhat distended or tympanitic." In 12 cases (Nos. 14, 19, 28, 32, 35, 38, 39, 40, 43, 47, 48, 50) the abdomen was not distended. In most of these cases "rigidity without distention" was present. In one or two cases the abdomen was considered normal. In 4 cases (Nos. 11, 18, 23, 29) the abdomen was retracted, flat, or scaphoid. In one (No. 16) there was distinct retraction or concavity in the epigastric region with great distention over the transverse colon. In 3 cases (Nos. 11, 36, 37) there is no record found of the condition of the abdomen. In 7 cases (Nos. 8, 9, 13, 21, 33, 34, 49) perforation occurred before admission.

Conclusions. While distention is present in about half the cases analyzed, it is not an early but a late manifestation of perforation. In some few cases (*i. e.*, with necrosis and the dropping out *in toto* of the slough) distention may be important.

Liver Dulness. In 12 cases (Nos. 3, 7, 11, 15, 16, 22, 26, 28, 43, 45, 48, 50) liver dulness was present; in 5 cases (Nos. 3, 17, 23, 25, 46) it was much diminished; and was absent altogether in 5 cases (Nos. 6, 14, 36, 42, 44). In the remaining 28 cases 7 are without previous history (already mentioned) and 21 have no record of the condition of liver dulness.

Conclusions. In the 22 cases available for study the liver dulness was present in its usual proportions in 12 cases and much diminished in 5, a total of 17. In these last cases the dulness was usually gone in the midclavicular line and present in the midaxillary line. It was totally absent in but 5 cases. It cannot therefore be relied upon as a very valuable clinical sign of perforation, especially as perforation is apt to occur in a considerable proportion of the cases in which decided meteorism is already present with great or almost total destruction of the normal liver dulness.

Important General Symptoms. I am not certain that there are any general symptoms that are most important. Two, however, deserve some consideration because they have been urged upon us by those high in authority in the medical world—viz., hemorrhage and chills. Mitchell and McCrae[1] in their study of the perforative cases at Johns Hopkins Hospital noted the frequency of perforation with hemorrhage. Hemorrhage was present in 2 out of 8 of their cases. In this study, however, large hemorrhage or hemorrhages preceding or at the time of perforation occurred in but 5 cases (Nos. 10, 25, 27, 40, 48). In 3 other cases, however, small hemorrhages occurred during the illness, and in two cases a large hemorrhage (Cases XXIX. and XXXIX.), but seemed to have no relation to the perforation. In 33 cases there was no hemorrhage of any description, while there is no good previous history in 7 cases. In a recent comprehensive article Goodall (*Lancet*, July 2, 1904) found that shivering or chill at or within an hour or two of perforation were present in 26 per cent. of his cases. In this study there was no chill or shivering in 32 cases; in 4 cases chills were present early in the disease or at a time bearing no relation to perforation; in 7 cases chills were present at or about the time of supposed perforation. In 33 cases, therefore, or 66 per cent., no hemorrhage from the bowels occurred. In 7 cases with no history there is no record of bleeding previous to admission to the hospital. This brings up the actual number of cases without hemorrhage to 40 or 80 per cent. In 5 cases, or 10 per cent., large hemorrhage or profuse bleeding preceded the perforation or was occurring at the time when perforation was suspected. In 2 such cases the diagnosis of perforation was not made; in 1 (No. 40) it was considered but negatived, and no operation done; in the second (No. 27) operation was performed solely to check hemorrhage and perforation found. Chilliness or chills were present in but 14 per cent. of the cases. Shivering when present does not, in my experience or in the analysis of these cases, make one especially suspicious of perforation, though with other corroborative signs it is one more aid in a probable diagnosis.

Study of Temperature at Time of Perforation. No change noted in 15 cases; slow fall with subsequent rise of temperature in 10 cases; immediate fall and subsequent rise, 4 cases; immediate rise with subsequent fall, 2 cases, no temperature data, 5 cases; no history, 7 cases; and no fever at time of perforation in 2 cases.

Analysis. In 15 cases no changes in the temperature were noticeable, that is to say, there were present the usual daily variations in fever, such as is present in typhoid. There were no unusual variations, and as it is customary when perforation is suspected to stop bathing, etc., treatment has nothing to do with such variations. In 5 of the cases there was an immediate fall in temperature, sometimes, as in Cases XXVII., X. and XXXVII., amounting to three or four degrees, followed by a rise, a condition of temperature simulating that of intestinal hemorrhage. In 10 *cases there was a slow fall in temperature, lasting from a period of eight to twelve hours*, but usually bringing down the temperature to normal or subnormal, with a subsequent reaction. The total drop here may be large, *some four to five degrees.* This I consider the most important fact developed from the

[1] Johns Hopkins Hospital Reports, vol. x.

study of the temperature in these cases. In 2 cases there was immediate rise with subsequent fall and in 5 a slow rise with subsequent fall. In 5 no temperature records can be found, while in 7 the perforation occurred previous to admission. In 2 there was no fever at the time of perforation, nor did perforation produce any special change in the chart.

Study of the Leukocytes. The leukocytes rose above normal in 10 cases; there was a fall in 3 cases; no change in leukocytes occurred in 14; no counts were made in 16 cases; and no previous history was given in 7. In Case XXV. the leukocyte count was 22,000; in Case XIV. it was 17,500, 16,500, 13,400, made at intervals of several hours; in Case XVI. the leukocyte count rose from 8680 to 13,100; in Case II. to 12,440. In 2 cases, Nos. 15 and 37, the counts were respectively 11,360 and 11,500, the latter three hours after perforation. In 2 cases, Nos. 11 and 38, the leukocytes were 9600 and from 5400 to 9400 respectively. In 2 cases, Nos. 5 and 26, the count rose from 4900 to 7080, and again fell to 4950; in the latter case from 5600 to 7200. In those cases in which the fall of leukocytes occurred, as for instance Case XLV., the count fell from 7200 to 2900, and in Case XLVIII., in which several days previous the count was 19,000 after perforation, it was 6300 and 5900. In the 14 cases in which no change is recorded the average count was in the neighborhood of 5000, 6000, or 7000 leukocytes. In but 1 case, No. 43, was the count below 4000.

Analysis. In 16 cases no record of leukocyte counts can be found in the history, and in 7 cases there is no previous history. This total of 23 cases, or almost half the total number, are worthless as far as any study is concerned. In 14, or 51.8 per cent. of the remaining 27 cases, there was no change observed in the leukocyte count; that is, no increase or decrease of such character as to give any additional weight or aid in diagnosis. In 10 cases, 37 per cent., there was a distinct rise in the number of leukocytes and decided increase in several cases (Cases XIV., XV., XVI., XXV.), yet in at least one or two of these (No. 25) it was evident that the patient had general peritonitis and the leukocytosis was of no diagnostic value. Indeed, I have noted a tendency in not a few cases to a small or decided rise in the leukocytes with a rapid fall to or near normal within twenty-four hours after perforation is suspected. In a disease characterized by a leukopænia it is difficult to properly interpret the behavior of the leukocytes, especially in the light of previous serious hemorrhage of the bowels (Case XLVIII.) or abdominal section (Case XVI.) or in suspected phlebitis, cholecystitis, or pneumonia (Case III.). In 3 cases, 11 per cent., there was a decided fall in the leukocytes, but little in each case, and in none sufficient to be of any service other than confusing the diagnosis (Cases III., XLV., XLVIII.).

The factors in the production of the leukopænia present in typhoid fever are still open to absolute proof, although the investigations of Fraenkel, Mallory, and Longcope have done much to enlighten us on the probable causes.

From Longcope's recent study, made at the Ayer Clinical Laboratory, the findings of Fraenkel and Mallory are corroborated, and the conclusion is probably warranted that in the bone-marrow changes are to be found the basis of the blood picture in typhoid fever. In typhoid fever, whether complicated or not by perforation or other lesions, usually producing in other infections an acute leukocytosis, the lack of the non-granular variety of leukocytes is noted; that is, there are active degenerative foci in the bone-marrow and differential counting shows about an equal proportion of granular myelocytes and clear lymphocytes, the former being the antecedent of the ordinary polymorphonuclear cells. In typhoid fever this usual proportion is reduced and when complications occur there are no polymorphonuclear cells to respond to the increased call made upon them. Recently the clinical side of this fact has been well brought out by the studies of Kast and Gutig, who have called attention to the lack of a leukocytosis in complicating conditions in typhoid; a year or two ago this same fact was pointed out in an article by Morris J. Lewis and Robert G. Le Conte, of the Pennsylvania Hospital, with special reference to suppurative ovarian cysts in typhoid fever.

Diagnosis. The diagnosis of perforation was made in 37 cases. The diagnosis of appendicitis or peritonitis was made in 6 cases; perforation was entirely unsuspected in 7 cases. In 2 cases hemorrhage was very severe and 1 was operated upon for the relief of the same and perforation found. Those cases diagnosed as peritonitis or appendicitis were usually brought to the receiving ward of the hospital with a history such as one would expect under the circumstances, usually of illness of but a day or so duration, and with but little history beyond this.

Operation. Operation was performed upon 39 cases, with 12 recoveries. In 11 cases no operation was done and all died. In at least 4 of the cases dying subsequent to operation death would certainly be attributed to causes other than the perforation. Two of them (Cases XXXVII. and XXXIX.) died from secondary perforation of other ulcers; a third case (Case XLIX.) died from sepsis due to double parotid bubo two weeks after operation; while the fourth (Case XXVI.) died of basal pneumonia eight days after operation. One case (Case XXX.) showed extensive sive thrombosis of the iliac vessels.

The non-operative cases need a word of explanation. In 3 the diagnosis was made but no operation permitted, or the case was considered too hopeless to be touched. In 7 the condition was unsuspected and operation never considered. The perforation was discovered at autopsy. One of the above cases was moribund on admission, the diagnosis was uncertain and operation impossible.

The 7 *undiagnosed cases* are of decided interest in this study (Nos. 16, 22, 27, 32, 35, 36, 50), and something can be learned from them.

Case XXII.—This case was thought to be an interstitial myocarditis with secondary hepatic and renal changes; but the absence of any fever, without any intestinal symptom caused the enteric feature to be entirely overlooked; he was semiconscious, with rather muttering delirium, and if he had pain did not complain of it. The abdomen was tender, however. Not until autopsy developed a fibrinopurulent peritonitis, with a perforation in the appendix due to typhoid ulceration, was the error realized.

Case XXVII.—The typhoid was easily recognized and operation done to control the frightful bleeding from the bowel; he poured blood per rectum for six days; operation revealed an unsuspected perforation in the ileum.

Case XXXII. presented physical signs of extensive right-sided pulmonary infiltration and softening; a few days before his death he had three or four liquid stools in each twenty-four hours; his temperature had come down and no abdominal symptoms were complained of. Autopsy showed severe deep ulcerations in the ileum and three closed perforations.

Case XXXV. was recognized as typhoid. Apparently mild type, with temperature down by the fifteenth day to 100° or lower; pulse was good; blood was noticed in stools this day, and in the next forty-eight hours the patient failed rapidly without any symptoms being noted as indicating any abdominal complication. He grew stuporous and died. At autopsy a perforation in the ileum was discovered, with general fibrinopurulent and hemorrhagic peritonitis.

Case XXXVI. —Typhoid readily diagnosed; hemorrhage on the sixteenth and eighteenth days, which was followed by distention and rigidity of the abdomen; no local tenderness. The pulse had always been rapid; the distention increased, while the rigidity diminished, and perforation was not considered. Death on twentieth day. Autopsy showed gas and feces in abdomen, general peritonitis, and four perforations.

Case L.—Typhoid diagnosed. Had congested bases, with delirium; became weaker, yet without symptoms of any special abdominal complication, and died on the twenty-second day from a supposed toxæmia. Autopsy showed a bronchopneumonia and a general fibrinopurulent peritonitis due to perforation in ileum 20 cm. above the cæcum; extensive ulceration in cæcum.

Case XVI.—A typhoid beginning acutely and on twelfth day developed an acute appendicitis. Operation. Poor healing of wound, followed by chills and phlebitis. On the twenty-eighth day severe localized pain to left of umbilicus, with extreme tenderness and great distention of transverse colon; pain and distention recurred at intervals in next forty-eight hours. Collapse of temperature, vomiting, etc., which were attributed to dressing of wound, but probably due to rupture of ulcer in colon on thirtieth day, which was not recognized. Final rupture on the thirty-sixth day; operation; death.

Typhoid recognized, Nos. 27, 16, 35, 50.
Hemorrhages, Nos. 40, 27, 35.
Toxæmia, No. 50.
Typhoid unrecognized, Nos. 22, 32.

Study of ten cases diagnosed as perforation but diagnosis disproved either at operation, at autopsy, or at recovery.

Number of cases	10
Operations	7
No operation	3
Recovered	6
Died	4

In the series of 7 operative cases 3 out of the 4 deaths occurred. Of the 3 non-operative cases 2 recovered and 1 died. I shall attempt no analysis of the symptoms in these cases except to state that in each there were clinical signs of such intensity as to warrant the diagnosis of perforation and recommendation of operation. In 2 cases "appendicitis" was mistaken for perforation; both patients operated upon with 1 recovery and 1 death. In 2 cases left basal pneumonia was mistaken for perforation; operation; both recovered. In 2 cases "gastritis" and "enterocolitis" were mistaken for perforation; operation was strongly recommended in one and refused, strongly considered in the second but finally decided against; both recovered. In 2 cases no cause could be discovered to account for the symptoms; one was septic with suppuration about the knee and hip-joint (iliac thrombosis?); operation; no perforation; while the second was a hemorrhage case with severe abdominal pain and distention. Operation; no perforation. The first died, the latter recovered. In 1 case Zenker's degeneration was present in the right rectus muscle. This man lived seven days after operation, at which time he was very toxic. He did not seem to die as the result of his surgery. In 1 case healed perforation with secondary rupture was diagnosed. The primary perforation was supposed to have occurred about the fourteenth day. Operation was recommended but refused. The man recovered, left the hospital, and developed on the forty-eighth or fiftieth day a sudden peritonitis, with death in twenty-four hours. This was considered perforation of the colon.

A study of the cases that recovered.

These cases are Nos. 7, 8, 9, 11, 14, 21, 34, 35, 38, 41, 42, 43. It is curious and interesting to note that the cases that recovered seemed to go in groups, the first batch to recover occurring early in 1902 and in rather rapid succession; then a series of fatal cases occurred followed by a batch of fairly successful cases. Since May, 1904, not more than 7 have perforated and none of these have survived the operation. Two cases (Nos. 8 and 34) did not regard themselves as ill

at the time the symptoms of perforation occurred. Four cases (Nos. 14, 21, 41, 43) were considered mild attacks of typhoid. Six cases (Nos. 7, 11, 35, 37, 38, 45) were considered severe infections. The time elapsing before operation was very different in different cases; in Case VII., twelve hours; in Case VIII., twenty-four hours; in Case XIV., eight hours; in Case XXXV., twenty-four hours; in Case XXXVIII., five and a half hours; in Case XLI., seven hours; in Case XLII., eight and a half hours; and in Case XLIII., from forty-eight to sixty hours. In 4 cases (Nos. 9, 11, 21, 34) operation was performed as soon as possible after admission to the hospital. These were cases in which the symptoms of peritonitis were evident upon their admission to the receiving ward, and which after having been seen by the attending surgeon were transferred at once to the operating room. Operation seemed to have little or no no effect upon the general course of the disease. Case VII. went through a prolonged serious illness, having three relapses; Case IX. had two relapses, while Case XXXVIII. had one relapse. Case IX. left the hospital with an operative hernia which he refused to have repaired. Case XLII. developed a fecal fistula some two weeks after operation which subsequently healed. The surgical results in the remaining cases were good.

Age. Two cases were boys of thirteen; 1 case, fourteen; 1 case, eighteen; 1 case each of the following ages: twenty-one, twenty-eight, thirty, thirty-seven, thirty-eight, forty-two, forty-three, forty-nine. All the recoveries were in boys and men. There were eleven whites and one black.

Case VIII. walked to the hospital. It is probable his perforation occurred one month after convalescence from a primary attack; he had no symptoms of a relapse. Case XXI. was diagnosed as appendicitis, while Cases IX. and XXXIV. were considered simply as peritonitis.

Conclusions. No case need be despaired of after operation (see Case VII.). Cases that come to the receiving ward walking in or being brought twenty-four hours after symptoms of perforation make up 25 per cent. of the recoveries. The hemorrhage cases accompanied with perforation proved uniformly fatal even though the perforation was caught very early. Relapses after operation occurred in 25 per cent. of the cases recovering.

Diagnosis. The diagnosis of perforation rests upon a comprehensive knowledge of typhoid fever and the proper interpretation of the clinical signs previously mentioned. The immediate local signs are sudden, severe, localized, or general pain, either continuous or paroxysmal, followed by tenderness and rigidity. The onward march of these symptoms is of importance. The abdomen primarily is not at all, or much, altered in contour. It is apt to be flat or round, soon becoming tender and rigid. Distention is not usually an early symptom, but appears six or eight hours after perforation. Chills, vomiting, sweats, and rise or fall in temperature may be present and be of some aid. In not a few cases no such symptoms are noted and the pulse and respiration show no alteration in rate. Two things must be remembered in regard to the patient: (*a*) A previous flabby and pendulous abdomen may show no muscle rigidity even though peritonitis is beneath it; (*b*) a certain proportion of cases perforate and yet make no complaint of abdominal pain or tenderness. In such cases if other complications can be excluded, perforation should be carefully considered (see the undiagnosed cases). The study of the leukocytes is of no positive value. It is in some cases of negative value. When other signs are positive there is often no leukocytosis. When the diagnosis is very doubtful not infrequently a leukocytosis is found, usually due to causes other than peritonitis. Auscultation of the abdomen may aid by the absence of peristaltic sounds, and the presence of the breath sounds which can be heard, if perforation is present, to an unusual intense degree. Stengel has confidence in this sign.

Lastly, the presence of a secondary pneumonia is very apt to obscure the proper diagnosis. I know of no way to avoid mistakes under such circumstances. Two cases of this series (Nos. 3 and 24) presented this condition which led to hesitation on the part of physician and surgeon, yet in each perforation had occurred.

The conditions most likely to be mistaken for perforation are basal pneumonia, pleurisy, extensive meteorism, cholecystitis, hemorrhage followed by pain and rigidity, enterocolitis, gastroenteritis, phlebitis, especially iliac and less commonly femoral, more rarely pericarditis and acute cystitis. Appendicitis occurring during typhoid and perforation of a mesenteric gland necessitate differentiation from perforation, but each requires operation.

Bacteriology of Peritoneal Exudates.

In the series of 50 cases it is to be regretted that careful systematic investigations of the peritoneal fluid were not made. In many of the cases, however, the sudden development of the symptoms and the haste of operation prevented. In some few cases cover-slip examinations only of the fluid were made; altogether I find but 18 bacteriological examinations of the peritoneal fluid having been made, and of them three are not included in my series of cases, that is, they occurred since June, 1904. It is sufficient to say that the predominating bacillus secured by culture was the bacillus coli. This was present alone in 8 cases. In 2 cases there were cross-cultures of streptococci, pyogenes aureus, and staphylococci on the one hand, and in the other case, streptococci, staphylococci, and bacillus coli. In 3 cases there were plain cultures of staphylococcus and streptococcus respectively, and by cover-slip streptococcus in the third case. The bacillus lactis aërogenes and bacillus proteus vulgaris were found in one case (Case XXII.); streptococci, bacillus coli, and typhoid bacillus in one case (Case XXV.); and in

another case staphylococci, streptococci, and bacillus lactis were found (Case XLI.). In 1 case an unidentified bacillus was discovered (Case XV.). In 1 case (not in table) the exudate was sterile, and in 9 cases which came to autopsy I can find no record of cultures having been made.

Conclusions. The bacillus coli communis would therefore seem to be the organism most frequently present in the peritoneal exudate in our cases.

conclusions.

1. Perforation of the bowel in typhoid fever is more common than is generally supposed, occurring once and a trifle over in every three deaths.

2. The most common time of perforation is between the fourteenth and the twenty-first days. In 92 per cent. of the cases in this series the perforation occurred between the second and fifth week inclusive. The earlier cases are probably perforation in a relapse; now and then perforation may occur without evidence of previous illness.

3. Perforation occurs in cases of all grades of severity, from the ambulatory to the hemorrhagic type. It is most common in those with moderate (25 per cent.) and severe (50 per cent.) infection (75 per cent.). It is not more common in the hemorrhagic than in the mild cases (8 per cent. each).

4. The ileum is the common site of perforation (86 per cent.); the majority occur within twelve inches of the ileocæcal valve; the appendix and colon respectively are the next most frequent sites of perforation in this series of cases.

5. Pain of some kind is present in 75 per cent. of all cases. In 50 per cent. of the cases the onset is sudden and severe and of increasing intensity, localizing itself to a special zone. In 20 per cent. of the cases the pain is of slow onset, not localized, with general distribution. In some cases (12 per cent. of this series) no pain is complained of, and the usual symptoms of perforation are absent.

6. Tenderness and rigidity are present in from 75 to 65 per cent. respectively of all cases, and are usually combined; in some cases either one or the other may be wanting; rigidity especially may be absent in cases with rather a pendulous and relaxed abdominal wall.

7. When perforation is suspected the temperature should be taken every hour; only by this means can the immediate rise and slow fall to normal or subnormal which often occurs be detected; in some cases, and especially those of extreme toxicity, no noteworthy change at all in the pulse, temperature, or respiration can be detected when perforation occurs. Diagnosis is then only an inference.

8. Distention (if absent during the course of the disease and at the time of suspected perforation) is a late symptom of perforation. The obliteration of liver dulness is not a reliable sign of perforation.

9. The study of the leukocytes is of little aid. In a few cases their increase is such as to assure you of your diagnosis. In a considerable number of cases there is a decided reduction in leukocytes after symptoms of perforation. Differential counting is not of practical use.

10. Before being assured of our diagnosis right-sided pleurisy, pneumonia (especially in the young), cholecystitis, acute gastrointestinal indigestion, femoral and iliac thrombosis, appendicitis, peritonitis without perforation, cystitis, rupture of a mesenteric gland, or even hemorrhagic exudation into the abdominal muscles (Zenker's degeneration) should be considered. Even then mistakes in diagnosis will be made.

11. While nature will infrequently close one, two, or even three perforations, the only rational procedure when perforation occurs is operative interference. No case is too desperate for the attempt. Not infrequently the so-called mild cases succumb, while very ill ones recover.

12. The diagnosis made, time for operation has arrived; its important point is rapidity. Closure of the perforation and drainage is all that is needed; fifteen to twenty minutes should suffice.

(To be continued.)

THE USE OF IODIDE OF SILVER IN URETHRITIS.

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and

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It is not without a certain amount of trepidation that the subject of new remedies for urethritis is approached, realizing, from a careful perusal of the case-books of the Genito-urinary Dispensary, that nearly every drug in the Pharmacopœia, from quinine both up and down the scale has been used with varying results.

We have found no mention of the iodide of silver; that, however, was not what directed our attention to it.

In trying in various ways to decolorize a certain fairly efficacious silver preparation, the chief objection to which was its extreme filthiness, we stumbled on iodide of silver, and have been so impressed with its worth that we feel that our results should be made known.

Iodide of silver has been used very little in medicine; in fact, is not even mentioned in many works on therapeutics; but it is used quite extensively in photography. It was used experimentally in syphilis, but soon abandoned.

As iodide of silver is not soluble, it therefore became necessary to suspend it; this was found to be best accomplished in mucilage of quince seed.

The advantages over the various proprietary silver salts is that it is not proprietary, and that the exact strength can be controlled as the strength of nitrate of silver can be controlled. Our experience with the proprietary salts is that they vary considerably in strength, in addition to which is the fact that their exact composition is unknown.

The advantages over the nitrate are that the iodide does not stain and is less irritating, which permits of stronger solutions being used and the resulting benefits obtained thereby.

We are not putting forth the claim that it will work wonders, or that urethritis is reduced by it to the class of trivial complaints; but it can be said for it that it does reduce the acute stage to a minimum, and that it relieves the acute symptoms almost immediately.

It is possible to commence the local treatment at once, and with no bad results.

A few cases have been selected from somewhat over a hundred treated both in the office and at the Genito-urinary Dispensary of the University Hospital, it not being necessary to give the entire series of cases, as this would be simply reiteration.

The success attained in treating dispensary patients with this remedy speaks more for it than the success in practice, as dispensary patients are somewhat lax in their observance of directions as to their mode of life during the disease, and also from the fact that most of them do manual labor, usually heavy, which is not the ideal condition under which to treat urethritis.

Case I.—J. H. B. No previous attack of gonorrhœa.

March 4, 1905. Duration, one day; incubation, five days. Ardor urinæ; profuse purulent discharge; gonococcus present; 5 per cent. given four times daily.

7*th*. No ardor urinæ; discharge lessened; first urine cloudy; second urine clear; no urinary symptoms; 5 per cent. continued.

11*th*. No discharge; shreds in first urine; 5 per cent. continued.

18*th*. No discharge; very few shreds; 10 per cent. given twice daily.

25*th*. No discharge; no shreds. No treatment.

April 4*th*. No discharge; no shreds. No treatment.

11*th*. No discharge; no shreds. Cured.

Case II.—W. L. C. No previous attacks of gonorrhœa.

February 22, 1905. Duration six weeks; now has arthritis of left wrist; first urine shreddy; no discharge; 5 per cent. iodide of silver given t. i. d.

26*th*. First urine shreddy; shreds diminished; 5 per cent. t. i. d.

March 3*d*. No shreds; arthritis improved; 5 per cent. t. i. d.

10*th*. No shreds; no pain in wrist. No treatment.

15*th*. No shreds; joint much decreased. No treatment.

24*th*. No shreds; good function in wrist. Cured.

Case III.—Y. S. No previous attack.

February 12, 1905. Duration one year and a half; treatment spasmodic; shreds in both urines; patch in deep urethra; 5 per cent. iodide silver, with a deep urethral syringe.

16*th*. Shreds diminished; 5 per cent. deep injection.

19*th*. Very few shreds; 5 per cent. deep.

23*d*. No shreds; 5 per cent. deep, on account of the long-standing lesion.

March 3*d*. Urine clear; 5 per cent. deep.

8*th*. Urine clear; 5 per cent. deep.

11*th*. Urine clear. No treatment.

22*d*. No shreds. Cured.

Case IV.—Gonorrhœa one year ago; was thought well.

March 18, 1905. Now has shreddy urine. Granular patch at three and one-half inches; 5 per cent. deep injection.

22*d*. Fewer shreds; 5 per cent. deep.

25*th*. Few shreds; 5 per cent. deep and No. 30 French steel sound.

29*th*. No shreds; 5 per cent. deep; No. 30 sound.

April 3*d*. No shreds. No treatment.

12*th*. No shreds. No treatment.

20*th*. No shreds. Cured.

Case V.—E. S. S. Gonorrhœa one year ago.

January 17, 1905. Incubation six days; duration ten days; profuse purulent discharge; ardor urinæ; first urine cloudy; second urine clear; gonococcus present; 5 per cent. silver iodide hand injection given.

21*st*. No discharge; first urine shreddy; 10 per cent. injection.

31*st*. No discharge; few shreds; 10 per cent. injection.

February 24*th*. No discharge; no shreds. No treatment.

Patient left Philadelphia, and was not seen again until April 30, 1905, when the urine showed no return.

Case VI.—W. M. H. No previous attack of gonorrhœa.

December 21, 1904. Duration two days; incubation eight days; profuse purulent discharge; first urine cloudy; second urine clear; gonococcus present; 10 per cent. hand injection.

24*th*. No discharge; urine shreddy; 10 per cent. continued.

31*st*. No discharge; few shreds; 10 per cent. continued.

January 4, 1905. No discharge; no shreds. No treatment.

12*th*. No discharge; no shreds. Cured.

Case VII.—W. L. S. Gonorrhœa six months ago.

January 12, 1905. Duration four days; incubation one day; moderate discharge; no gonococcus found; diagnosis catarrhal urethritis; first urine cloudy; second clear; 10 per cent. hand injection given.

15*th*. Urine clear; no discharge.

Case VIII.—H. H. Gonorrhœa three times.

January 16, 1905. Duration six months, during which time he has not been under treatment regularly. Has been on periodic sprees. Now has frequent and imperative urination; purulent profuse discharge; both urines cloudy. Treatment balsams and irrigation, with either permanganate of potash or 1 : 4000 nitrate of silver every other day until February 25, 1905, when he was given a deep injection of iodide of silver 5 per cent.

February 28*th*. Frequency and urgency diminished; urine cloudy; discharge lessened; 5 per cent. deep.

March 3*d*. Urination normal; no discharge; few shreds; deep, 5 per cent.

14*th*. No discharge; urination normal; few shreds; 5 per cent. deep.

18*th*. No discharge; no shreds. No treatment.

25*th*. No discharge; no shreds. Has been drinking large quantities of beer. Cured.

These few cases speak for themselves, but, in conclusion, we would like to emphasize particularly the fact that the ardor urinæ usually subsides within twenty-four hours, and the discharge disappears well within a week.

The solutions cause absolutely no burning and no irritation. Indeed, not a single patient has complained of discomfort.

In cystitis of prostatic origin or after prostatectomy, we have found that it yields excellent results.

We should very much like to have it taken up in the other clinics. It has been used to some extent in eye work, and given good results.

It has been used in surgery in cases where silver was indicated, and it has done excellent work; the patients have not complained of a burning sensation when it was applied.

STUDIES ON CELL GRANULA AND AMŒBOID MOVEMENTS OF THE BLOOD CELLS OF LIMULUS.

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(From the Pathological Laboratory of the University of Pennsylvania and the Marine Biological Laboratory, Wood's Holl, Mass.)

(Concluded from page 52.)

If we now consider the bivalent cations, we find that $CaCl_2$, $Ca(NO_3)_2$ and $MgCl_2$ act similarly to NaCl. The changes in a $CaCl_2$ solution are, however, still more pronounced than in a NaCl solution. In a $\frac{1}{2}$ m. $CaCl_2$ solution the salts lose their granules, become entirely hyaline and send out many sharply pointed pseudopodia. In the course of several hours, even the cells which are suspended in the fluid, and which in the beginning had still been granular, lose their granules. In a $\frac{1}{2}$ m. $BaCl_2$ solution, however, in which the blood plasma forms a marked precipitate, the cells usually remain round, send out only few pseudopodia, and remain partially granular or become hyaline.

In $\frac{1}{2}$ m. $MnCl_2$ the granules are lost. The hyaline cells form a network, which, however, is not as strongly retracted as in $CaCl_2$. The individual cells do not send out as many processes as in $CaCl_2$, and they assume the shape of small balls or ereseents. In $\frac{1}{2}$ m. $NiCl_2$ we find masses of small hyaline balls. Frequently, probably one small ball corresponds only to a part of the cell. Besides, however, there are present round hyaline and a few granular cells. In $\frac{1}{2}$ m. $CdCl_2$ the cells are oval without granules, and around the nuclei the cells are frequently swollen. The nuclei are very distinct and somewhat gran ular. No pseudopodia are formed. In $\frac{1}{2}$ m. $Zn(NO_3)_2$ the cells are round to oval. The nucleus is clearly visible. The granules are entirely lost or only partially preserved. No pseudopodia are sent out. In $\frac{1}{2}$ m. $ZnSO_4$ we find round, somewhat swollen cells, which usually have lost their granules. At places where the precipitate formed does not cover the cells, no pseudopodia are formed. In $\frac{1}{2}$ m. $CuCl_2$ the cells are round or oval, without processes, and partially granular. In $\frac{1}{2}$ m. $BeCl_2$ we find many round and oval cells, with many granules. The periphery of the cells is sometimes free from granules.

We see, therefore, that manganese and nickel act in a similar way as calcium, although the number of processes is much smaller, especially if a solution of nickel is used. In the case of the other salts mentioned above, the processes are entirely wanting. The cell is partially fixed in its shape. Granules may or may not be present. In these salts ($CdCl_2$, $BeCl_2$, $CuCl_2$, $Zn(NO_3)_2$, $ZnSO_4$, $BaCl_2$) the precipitate formed with the blood plasma is very copious. How far this circumstance determines the character of the cells in these solutions cannot yet be decided.

Of the trivalent cations, aluminum has been examined. Al_2Cl_6 preserves the cells very well. They are usually round or oval. The granules are well preserved. In $\frac{1}{2}$ m. and $\frac{1}{4}$ m.

Al_2Cl_6 a visible precipitate is formed. In $\frac{1}{4}$ m. Al_2Cl_6 the precipitate formed is only microscopically visible. The cells and granules are, nevertheless, well preserved in the latter solution. In $\frac{1}{2}$ m. Al_2Cl_6 the cells become brittle. In $\frac{1}{8}$ m. Al_2Cl_6 they are somewhat swollen and much softer. In the last-named solution a part of the granules may afterward disappear, probably under the mechanical influence of movements in the fluid. Among the organic acids citric and tartaric acids were tested, the former at the same time being a representative of a trivalent anion. In $\frac{1}{2}$ m. sodium citrate the cells are present as flat disks. They assume, therefore, a shape in which a large number of them are found to exist in the blood inside the body. They possess many granules. Part of the cells are bent. The nuclei are very clearly visible. The cells float freely in the fluid or form only feeble agglutinating cell masses. In $\frac{1}{4}$ m. sodium citrate the cells form either flat disks with granules or round balls containing granules. They are floating in the fluid or lie on the surface of the slide without sending out any processes. Although these cells are only very slightly sticky, they easily form agglutinating masses if the fluid is agitated by a needle. In $\frac{1}{2}$ m. potassium and sodium tartrate the cells are round. Many possess granules. In a few of them the granules have been lost. Only very small pseudopodia are sent out. We see, therefore, that the sodium citrate, which strongly inhibits the coagulation of the blood, preserves the cells very well. The tartrates are not as effective in this regard as the citrates. The fact that citrate solutions of different concentrations act in a similar way makes it possible to conclude that these salts act not only by their osmotic pressure.

We find that, of all solutions which have been tested so far, a $\frac{5}{8}$ m. or $\frac{1}{2}$ m. KCl solution imitates best the action of the blood plasma upon the blood cells. There is, however, a great difference between the composition of the blood plasma and a KCl solution. We must, therefore, conclude that the effect of this solution upon the cells is produced by means which differ from the action of the blood plasma. The similarity of the effect of the KCl solution and of the blood plasma applies, perhaps, only to certain visible changes, and these two solutions may act very differently in other respects upon the blood cells.

A number of experiments were made to determine whether combinations of different solutions act more favorably than an isotonic KCl solution. NaCl and KCl solutions were mixed in different proportions. In a similar way isotonic NaCl and KCl solutions were mixed with different quantities of $\frac{1}{2}$ m. $NaHCO_3$, $\frac{1}{2}$ m. NaH_2PO_4, $\frac{1}{2}$ m. KH_2PO_4, $\frac{1}{5}$ m. NaOH. In no case was a mixture found which acted more favorably than a $\frac{1}{2}$ m. or $\frac{5}{8}$ m. KCl solution. We find, therefore, that the neutral KCl solution acts similarly to the blood plasma.

A 2 per cent. to 10 per cent. solution of resorcin or 2 per cent. solution of hydroquinone or a weak solution of pyrrhol, in each case mixed with an equal quantity of a 4 per cent. NaCl solution, preserves the cells, which remain oval or round and preserve their granules. The cells do not send out pseudopodia. In a 10 per cent. solution of resorcin the cells are slightly or not at all sticky, cannot be easily drawn out, and the granules do not flow out of the cells if we pull the cells with a needle. It is, however, possible to transform the cell into a flat plate, in which granules are arranged in rows if we glide a needle over the cells. Chloroform added to a 4 per cent. NaCl solution prevents also the sending out of pseudopodia.

On the action of alkaloids and some other substances it is intended to report later.

Some further observations on the behavior of the granules on the nuclei of the cells, and on the consistency of the protoplasm of the blood cells of Limulus, may be added as a continuation of my former communications.

Cell Granula. We have seen in the foregoing that the granules remain preserved under the influence of alkalies, provided they are not so concentrated that they destroy the whole cell. We also saw that slightly acid salts, like KH_2PO_4, preserve the granules at least equally well; the addition of somewhat stronger acid destroys the granules. The latter disappear upon the addition of H_2O or in solutions of glycerin and of sugar, and the majority of the granules disappear in solutions of urea. Different neutral salts behave differently in this regard. We may recall the difference in the action of potassium and of sodium salts. In the blood plasma the granules are preserved for a long period. In all cases we find that the cells spread out on the surface of the glass lose their granules much more quickly than the contracted cells. This applies to the apparently spontaneous loss of the granules, as well as to those cases in which the granules disappear if H_2O is afterward added to the blood.

We find a certain parallelism in the action of the external conditions upon the shape of the cells and upon the formation of pseudopodia on the one side, and upon the preservation of the granules on the other side. In those cases in which many pseudopodia are formed and the cells are long drawn out, the majority of the granules are lost (NaCl and $CaCl_2$), and in those cases in which the cells remain round or oval (alkalies, KH_2PO_4, sodium citrate, aluminum chloride, aluminum acetate, the concentrated salt solutions), or in which the spreading out of the cells is less extensive (KCl, NH_4Cl, blood plasma), the granules remain better preserved. In certain strongly toxic substances, however, the cells may remain round or oval, and the granules can, nevertheless, be lost (acids and salts of certain heavy metals). The fact that alkalies exert a preserving influence upon the granules might, perhaps, justify the conclusion that the granules are not nucleo-proteids.

The cells which are collected in KH_2PO_4 and in $NaHCO_3$ do not lose the large majority of their granules, even if

they are kept twelve to fifteen hours in this solution upon the slide.

If we add to the cells whose granules have been preserved by a hypertonic solution of NaCl, by an isotonic solution of KH_2PO_4, $NaHCO_3$, NH_4Cl, K_2SO_4, NaI, afterward a surplus of distilled water, almost all the granules may disappear. A certain number of the granules, however, usually remain preserved.[1]

Water has the same action upon the granules of cells which have been previously ruptured by a needle, in which case the granules are embedded in a mass of protoplasm, which has entirely lost all characteristics of a cell.

It is a question of great interest whether the action of the solution upon the granules is a direct chemical action or whether it is an indirect one, taking place by the aid of enzymes. If the latter alternative is the correct one, the dissolution would be comparable to autolytic processes and may, perhaps, be regarded as an autolysis of granules. The latter possibility is especially suggested because of the fact that even in blood plasma the cells which spread out upon the surface of the slide lose their granules apparently spontaneously. It is conceivable that the causes leading to the spreading out of the cells and to the formation of pseudopodia produce simultaneously an enzymatic dissolution of the granules. The fact that granules which have left the cells behave similarly under the influence of certain reagents, like distilled water, as the granules inside of well-preserved cells, seems contrary to this explanation. It may, however, be that the enzymes are present in the granules themselves, and that their action is independent of certain vital phenomena of the cells. At present this view can only be regarded as an hypothesis. It may be that the granules present are extremely labile albuminous substances, whose dissolution depends upon very slight changes in their environment.

If, in the course of the spreading out of the cells, the granules disappear gradually, we see, after a certain period, in their place very small grains indicating the former position of the large granules. In a $\frac{5}{16}$ m. solution of KCl, this can, for instance, be observed after two hours and a half. These small grains are especially visible around the nucleus. It is different if the granules disappear under the influence of acids, as, for instance, of $\frac{1}{3}$ m. HCl. Under these circumstances granules disappear here and there quite abruptly, and nothing indicates the place where the granules had been situated before.

In one experiment a needle was glided over a spread-out cell which had been kept for two and a quarter hours in a 2 per cent. $NaHCO_3$ solution. The cell was transformed into a protoplasmic thread and a granulum was torn off. At the place where the granule had been fixed a very slight prominence was left. This seems to demonstrate that the granules consist of a rather tough substance.

As we have seen, the granules disappear apparently spontaneously after an addition of certain solutions. I could, however, never observe that two or more granules united to form one single structure during the process of liquefaction which necessarily preceded the dissolution. We have, therefore, either to assume that the products of the liquefaction diffuse at once into the surrounding liquid or that the cell protoplasm which surrounds the granules prevents their union. Not rarely, however, does it appear as if two or more granules had combined to form one structure of a greenish tint. This, for instance, is not rarely seen in blood cells which have been collected in combinations of $\frac{3}{8}$ m. NaCl and KCl and solutions of glycerin and urea which are isotonic with the salt solutions. In every case in which it appeared as if the granules had united, it was possible to demonstrate, by drawing out the cells by the aid of a needle, that the granules had remained entirely isolated and merely had approached each other so closely that they appeared as one single structure. By exerting a certain traction upon the cell, it was usually possible to demonstrate the granules as separate bodies. The optical illusion, however, is perfect in such cases.

Inside the cells the granules do not produce any Brownian movements. If, however, we draw out a cell with a needle, so that a widely diffused mass of granules is produced, we may see many granules to move very actively. Inside the cell it seems that the granules are packed together so closely, and are, perhaps, also surrounded by such a dense layer of protoplasm that such a motion is not possible. If we collect a drop of blood in a hypotonic salt solution, some cells may expand by taking up water. In the beginning the granules may still be preserved. Under these circumstances we may occasionally observe that a number of granules in such a cell are still fixed and that half the granules which are lying in the swelling cell free themselves sufficiently to be able to produce Brownian movements.

As we have seen before, it is possible to draw out cells which have been lying in hypertonic NaCl solutions into large masses of granules, provided the osmotic pressure of the solution does not exceed a certain limit. It is very easy to draw out cells which have been lying in 1 per cent. to 4 per cent. $NaHCO_3$ solutions into large masses of granules by the aid of a needle. Under these circumstances we see distinctly that the granules do not move quite freely in the fluid, but that they all are connected by a protoplasmic mass which can be easily stretched, and which, under the influence of the movements of the granules, is drawn out into fine threads. This protoplasmic mass permits the granules to become separated up to a certain limit, until the tension of the drawn-out protoplasm becomes so great that a further separation is not possible without the protoplasm being ruptured. A large number of granules remain spread out around

[1] It is intended to examine later how far purely mechanical factors are responsible for this fact.

the nucleus. Many others, however, flow away much farther. Only a certain portion become entirely free, the protoplasmic fibrils not being strong enough to keep the last-named granules in a fixed condition.

If the cell swells or becomes round, as it is usually found to do under the influence of mechanical irritations, as, for instance, if a cell falls upon a slide, we can clearly see that the granules are situated directly under the surface layer of the cell. We may, therefore, assume that they are strongly attached to this layer. This is also very clearly visible in a $\frac{5}{8}$ m. KCl solution to which has been added a little NaOH or a very small amount of HCl. In the latter case, however, many granules disappear within a short time.

In our former papers we have already mentioned that if a cell is drawn out into threads, the granules become frequently embedded in the threads.

Cell Nucleus. In the course of these investigations we repeatedly tried to gain some insight into the consistency of the nucleus by exerting pressure directly upon the nucleus by the aid of a finely pointed needle. We described before that if we draw out a cell into a fibre, the nucleus remains very visible as a small ball in the centre of the thread or may in other cases be drawn out into a long rod, no longer visible inside the fibre. If we try to press directly upon the nucleus —a layer of cell protoplasm probably separates in such a case the point of the needle from the nucleus—we find that it is possible to change the nucleus without the shape of the cell being markedly altered. The nucleus may, under the influence of pressure, lose its vesicular character and may resume a cylindrical shape. By applying renewed pressure, further changes of the form of the nucleus may be obtained. Such changes of form may be produced in cells which are surrounded by blood plasma, as well as in such cells which lie in distilled water or in solutions of glycerin. The nucleus, therefore, behaves in such cases not like a perfect liquid, because it does not resume its original vesicular shape after the pressure has subsided. One has even the impression that the nucleus is not very soft, but consists of a rather tough substance. We must, however, take into consideration that the difficulty to touch a small body like a nucleus with the point of a needle renders it possible that its resistance toward pressure is overestimated.

In certain solutions, as, for instance, in hypotonic solutions of potassium salts, the nucleus may very soon take up water and swell. Under these conditions granula become frequently visible within the nucleus, and it sometimes happens that a vacuole which is formed inside the protoplasm presses upon the nucleus, so that the nucleus surrounds, like a crescent, one side of the vacuole. This proves that, under these conditions, the nucleus is soft and easily adaptable.[1]

[1] In his Experimentelle Untersuchungen uber die Kerumembran, Beiträge zur path. Anat. (Bollinger Festschrift), Wiesbaden 1903, Albrecht assumes that the nucleus is quite liquid.

In such hypotonic solutions the nuclei do not all swell simultaneously. In a $\frac{1}{8}$ m. KNO_3 solution, it is, for instance, possible to see large, swollen nuclei in some cells, and in others small nuclei possessing a greenish tint.

A large variety of nuclei can be seen in hypertonic solutions of urea. Besides small, greenish nuclei, large, swollen, hyaline nuclei are visible, in whose periphery granula are situated. It is possible to observe changes caused by karyorrhexis. The peripheric part of the nucleus, which seems to possess a greater resistance, and which, therefore, may appear like a membrane, disintegrates into a number of granules, in which case the shape of the nucleus may at first be still preserved. Later we find granular, stellate, and rod-like nuclei. By the mechanical action of a needle which draws out the cells, such nuclei can be easily separated into masses of granules, which become included in the cellular threads in such a way that they are entirely invisible. The stronger solutions of urea appear, therefore, to exert very frequently a dissolving influence upon parts of the nucleus. We may assume that, besides the alkaline reaction of urea solutions, their permeability through cells which, according to Overton, is larger than the permeability of inorganic ions is responsible for this result.[1]

Consistency of the Cell Protoplasm. It is possible to cause the explosive disintegration of a rounded cell containing granula by a mechanical shock with the aid of a needle, or even under the influence of the motion of the liquid in which the cell has been suspended. After the surface layer, which offers a certain resistance, has been ruptured, the contents of the cell with granules and nucleus flows out and forms a soft, structureless mass. It is easily possible to produce threads out of this mass by exerting a certain traction or pressure. It is especially easy to cause the rupture of the cells in isotonic solutions of NH_4Cl and in urea solutions, provided the cells had preserved their round shape and their granules. In this case the consistency of the cell corresponds to that of a soft, almost liquid mass, which is surrounded by a surface layer which can be ruptured. This mass, however, does not disappear entirely in the surrounding fluid, but its consistency is such that it only permits of a limited expansion.

The constituent parts of the cell are less movable in hypertonic salt solutions and in certain toxic solutions. In a 4 m. NaCl solution, as well as in a 10 per cent. resorcin solution, it is no longer possible to draw out a cell with a needle, but such a cell can only be transformed into a plate by gliding over it with a needle.

In my former communications it has been shown that the cells can be easily drawn out into threads and that several cells may be united to form one single thread, especially if the cells have been kept in hypotonic or in weakly alkaline solutions.

[1] See Höber, Physikal Chemie d. Zelle u. d. Gewebe, Leipzig, 1902, p. 133.

To achieve this, it is necessary to overcome the elasticity of the cell. If the traction exerted is not sufficient to overcome the elasticity, the cell resumes its original shape after the tension has ceased. In solutions of urea, for instance, the cells are very elastic. The elasticity of the cells can be demonstrated if we remove cells which have already spread out from the surface of the slide by the aid of a needle. Cells which have been lying in a $\frac{5}{16}$ m. KCl solution for two and a half hours are suitable for this experiment. Under these circumstances we may observe that such a cell retracts and rounds off either to form a ball or to form an oval structure. In this case we have, therefore, to deal with a somewhat tough substance. The cell has, therefore, in order to spread out upon the slide, apparently to overcome its own elasticity. Another possibility which has to be taken into account is that this elasticity is only produced through the changes which take place during the process of the spreading out of the cell. It is very probable that the rounded, not yet spread-out cell has a consistency which differs very much from that of a spread-out cell. Certain observations mentioned in the former communication render this probable. The spread-out cells can easily be drawn out into very plastic, fibrin-like masses if we roll them between two slides. The fresh cells, however, tested immediately after the blood has left the animal, seem to be less plastic and not as soft.

Different, again, is the consistency of the pseudopodia which are sent out, for instance, after one hour in a $\frac{5}{8}$ m. KCl solution by those cells which are suspended near the glass. These pseudopodia appear to the touch of a needle not as soft but rather as solid structures. It is possible to move them a little to and fro. The excursions, however, are not very great. Their consistency may be compared approximately with that of a piece of gelatin which is a little swollen, but still solid.

In certain hypotonic solutions it is possible to observe that a large part of the cell protoplasm surrounds, as a hyaline swollen mass, the central part which contains the nucleus. If we cut off with a needle a part of such hyaline protoplasm, it rounds off. This, however, does not prove that we have to deal with an absolutely liquid mass, but the consistency in this case is probably more like that of mucus.

The majority of the cells which are surrounded by water or by solutions of urea or glycerin can no longer be made to explode. They form an elastic mass, which can be drawn out into fibres in a similar way as the cells which spread out spontaneously on the surface of the slide. Under these conditions the cells become sticky, through a change in the consistency of the protoplasm. They do not secrete the sticky substance, but the protoplasm itself changes its consistency.

It seems, therefore, to be characteristic for these cells that their consistency can be changed under different conditions.

In hypotonic salt solutions and alkaline solutions we may occasionally see hyaline structures leaving the cells, becoming round and moving around the periphery of the cell which they have left. Such structures seem to be very fluid. The variety of processes is still increased by the fact that it appears that the different parts of the cells may swell unequally under the influence of certain solutions. We see, for instance, that in isotonic and in certain hypertonic solutions of urea round bodies which still may contain granula are formed in the interior of the cell. They correspond to the endoplasm of the cell. The nucleus also is able to swell and to produce similar round bodies. Such bodies can also be formed in isotonic KCl and KNO_3 solutions from the endoplasmatic part which contains the granula. In hypertonic urea solutions, for instance, we may notice a distinction between an endoplasmatic granular and a round, concentric, exoplasmatic hyaline part in the course of the first or second hour. The margin between the two zones is distinct. In a similar way it is possible sometimes to produce, inside of five minutes, such a hyaline zone around the granular part of the blood cells, if we expose cells which in $\frac{1}{2}$ m. KNO_3 solutions had preserved their round and granular character to the influence of distilled water by pouring off the KNO_3 solution and by replacing it by distilled water. In cases in which urea or water have this effect, we have probably to deal with the swelling of parts of the cell. It remains still to be determined why such a sharp separation takes place between a granular endoplasmatic and a hyaline exoplasmatic part, instead of the water gradually and evenly penetrating into the intergranular protoplasm.

BOOK REVIEWS.

A Manual of Personal Hygiene. Proper Living upon a Physiologic Basis. By American authors. Edited by Walter L. Pyle, A.M., M.D., Assistant Surgeon to the Wills Eye Hospital, Philadelphia. Second edition, revised and enlarged. 12mo. volume of 441 pages; illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

Dr. Pyle's *Manual of Personal Hygiene* has evidently succeeded in winning for itself a place in the library of the physician, and probably of his patient also, as evidenced by the appearance of a second edition, thus showing the growing demand for such a book. In this edition, as in the first, Dr. Pyle has been assisted by a number of prominent American physicians, each writing upon his chosen specialty, and setting forth the means of health with a simplicity, conciseness, and authority that is rarely approached in a similar work. In this edition there have been added and fully illustrated a System of Home Gymnastics, by G. N. Stewart, of Chicago; a chapter on Domestic Hygiene, by D. H. Bergey, of Philadelphia, and an Appendix containing the simpler methods of hydrotherapy, thermotherapy, and mechanotherapy; also a chapter on First-aid Measures in Medical and Surgical Accidents and Emergencies. The book, already valuable at the time of its first appearance, has been made more so by these additions, and we feel that physicians, by recommending this book to their patients, are rendering them valuable service.

E. L.

Obstetrical and Gynecological Nursing. By E. P. Davis, M.D. Second edition, revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

This book contains 381 pages and many excellent illustrations. It is divided into two parts, Obstetrical Nursing and Gynecological Nursing. A better work on this subject it would be hard to find. All the possible duties of a nurse attending an obstetrical or gynecological patient are most carefully covered. It is a well-known fact that many physicians have different methods of doing the same thing. This is especially so in gynecology and obstetrics, still Dr. Davis has carefully selected in every case the best recognized methods and instructed the nurse in the same. Chapters IV., V., VI., and VII. are of especial excellence. These include the case of a normal labor case. Great attention is paid to asepsis throughout the work. All the possible accidents occurring in a labor case and the nurse's duty in each are carefully described, both when the physician is present or in emergencies when he is absent. The second part of the book is devoted to the nursing of gynecological patients, the various positions for examinations, and the local treatment; preparation for gynecological operations, preparatory and after-treatment of the patients. Preparation of the operating room and all its accessories including preparation of supplies, etc., is carefully gone over. One chapter is devoted to the duties of an office nurse. Chapter XII. is devoted to cancer, its suspicious symptoms, cancer of the pelvic organs, cancer of the breast, non-operative treatment of cancer of the bladder or bowels, bed-sores, pain, death from cancer, dangers of infection, danger to the nurse. Chapter XIII. gives a brief sketch of the menopause and of some of the most common mental diseases complicating pelvic disorders. Chapter XIV. gives a brief account of the symptoms and treatment of venereal diseases in the female.

The work is well printed; there are few typographical errors; the indexing is excellent. The book is one of the best of its kind that the reviewer has had the pleasure of seeing.

C. C. N.

The Practical Application of the Roentgen Rays in Therapeutics and Diagnosis. By William Allen Pusey, A.M., M.D., Professor of Dermatology in the University of Illinois, etc., and Eugene Wilson Caldwell, B.S., Director of the Edward N. Gibbs' X-ray Laboratory, University and Bellevue Hospital Medical College, New York, etc. With 176 illustrations. Pp. 591. Philadelphia, New York, and London: W. B. Saunders & Co.

Like most books of its kind, this is not one that can be used as a text-book for beginners in *x*-ray work, but it is a most valuable reference work for anyone interested in this particular branch of medical science. It is divided into two parts. In the first, Mr. Caldwell, unlike many authors of such books, does not dwell chiefly upon the particular forms of apparatus in which he is interested or uses at the expense of other forms equally as effective or better, but discusses the subject in a broad sense, dealing with the apparatus now in use in a general way, and as fully as is possible in a book of this size. The descriptions of many unique contrivances of his own design or of other operators are of value to any *x*-ray worker. In the second part Dr. Pusey has dealt in a thorough and up-to-date manner with the therapeutic uses of the rays and the technique of their application in the treatment of all pathological conditions in which they have been tried. His own conclusions as to the value of the rays in treating each disease, deducted from his own experience as well as that of other men of authority, and the reports of his own cases, render this book one of the most valuable works on this subject yet in print.

H. K. P.

B.J.C.D.

POST-GRADUATE COURSE

DEPARTMENT OF MEDICINE

UNIVERSITY OF PENNSYLVANIA

COURSES OFFERED TO GRADUATES IN MEDICINE DURING THE MONTHS OF MAY AND JUNE, 1905

ANNOUNCEMENT

The course will extend over a period not exceeding six weeks.

Beginning May 15, 1905, the University will conduct a spring course in Medicine, designed especially for practitioners, but open also, in the laboratory courses, to advanced students in Medicine. It embraces almost the entire curriculum of Medicine, and has been devised to meet the requirements of a wide group of practitioners and students of Medicine.

In designing the instruction offered in the spring course, the needs of the practitioner have been kept in view, and so far as possible the work has been made of purely practical character. While this feature is emphasized in the clinical branches and specialties, it has not been lost sight of in the laboratories. In all the courses the work is of a nature to appeal to the surgeon and general practitioner who wish to revive or complete their knowledge of certain subjects, and to advanced students in Medicine who may not have had opportunities to pursue these courses of study.

The number of attendants upon certain clinical courses will be necessarily limited, in order that close personal attention may be accorded the patients. This number will vary with the nature of the course; and the admission, under these circumstances, will be made in the order of application.

The schedule of hours for post-graduate study is so arranged that a comprehensive course may be taken without conflict of hours, and for this purpose the subjects have been divided into two groups:

Group I. is devoted entirely to Internal Medicine, including laboratory and clinical work, and to the following specialties: Pediatrics, Neurology, Ophthalmology, Otology, Rhinology, and Laryngology.

Group II. is devoted entirely to General Surgery, including Surgical Anatomy and Pathology, and to Gynecology, Obstetrics, Orthopedic Surgery, Genitourinary Diseases, and Dermatology

To those, however, who are desirous of devoting more time than is allotted on the schedule to any one subject, special courses and opportunities are offered for more advanced work.

LECTURE SERIES

MEDICINE

1. Medical Clinic. Dr. Tyson, in the Medical Amphitheatre, University Hospital, Saturdays at 9. A.M.

2. Medical Clinic, or Bedside Instruction. Dr. Musser, University Hospital, Thursdays at 12 noon

3. Medical Clinic, or Bedside Instruction. Dr. Stengel, University Hospital, Mondays at 12 noon.

4. Clinical Medicine. Dr. Fussell, in the Out-patient Department of the University Hospital, Thursdays at 1 P.M.

5. Clinical Medicine, with Especial Reference to Physical Diagnosis. Dr. Sailer, at the Philadelphia Hospital, Tuesdays, Wednesdays, and Fridays at 12 noon.

6. Clinical Medicine, with Especial Reference to the Diagnosis and Treatment of Diseases of the Gastrointestinal System Dr. Steele, University Hospital, Mondays at 1 P.M., and Saturdays at 12 noon.

7. Clinical Medicine, with Especial Reference to the Diagnosis and Treatment of Cardiovascular Diseases. Dr. Herman B. Allyn, at the Philadelphia Hospital, on Tuesdays, Wednesdays, and Fridays at 1 P.M.

8. Clinical Laboratory Methods. A course including Methods of Examining the Blood, Sputum, Urine, and Stomach Contents, to be given by Dr. William Pepper, at the William Pepper Clinical Laboratory, daily, from 11 A.M. to 12 noon, throughout the course.

9. The Treatment of Pulmonary Tuberculosis. Dr. W. B. Stanton, in the Pavilions for Tuberculosis of the Philadelphia Hospital, two afternoons a week.

PEDIATRICS

1. Clinical Instruction in the Diseases of Children. Drs. Griffith and Ostheimer, in the Wards of the University Hospital, on Wednesdays at 4 P.M., throughout the course.

2. Feeding in Infancy. Dr. Thompson S. Westcott, on Mondays and Fridays, in the Amphitheatre of the Children's Hospital, from 4.15 to 5.15 P.M., throughout the course.

This course will include the Modification of Milk. The Calculation of Percentage Formulæ. General Considerations of Substitute Feeding. Practical Application of Percentage Feeding. Weaning. Feeding in Difficult Cases. Dietetic Treatment of the Chronic Gastrointestinal Catarrhs. Various Expedients Necessary in Special Cases. Differential Modifications of Proteids, etc. Use of Cereal Preparations, Condensed Milk, etc. Clinical Cases Illustrating Nutritional Diseases: Rickets, Scurvy, Atrophy, Tuberculosis, Syphilis, and their Dietetic Management.

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1. Clinical Surgery. University Hospital, daily at 1 P.M., including operations in the Surgical Clinic, Surgical Diagnosis, Ward Rounds, and Demonstrations of the Modern Methods of Administering Anæsthetics.

2. Surgical Pathology. Dr. Müller, Tuesdays and Thursdays, from 11 A.M. to 1 P.M., at the New Medical Laboratories. This course consists in the demonstrations of the gross and microscopic lesions of the more common surgical affections, in so far as they apply to diagnosis and treatment.

3. Operative Surgery on Cadavers and Animals. Dr. Carnett. Mondays and Fridays, 11 A.M. to 1 P.M. This course will include Intra-abdominal Operations upon Animals (operations upon the Stomach, Gall-bladder, and Intestines), and such operations upon the Cadaver as cannot be demonstrated to advantage upon the Living Animal. The course will be arranged in accordance with the special needs of the Student. (Limited to ten.)

4. Surgical Anatomy. Dr. Davis. Mondays and Fridays, 2 to 3 P.M., Logan Hall. With especial reference to the anatomy of the peritoneal cavity, of fractures and dislocations, including demonstrations of methods of reducing dislocations.

5. Skiagraphy, Radiotherapy, and Phototherapy. Dr. Pancoast. Mondays, Wednesdays, and Fridays, 9 to 11 A.M. *X*-ray Department, University Hospital. Preliminary instruction in the various parts of an *x*-ray equipment, the handling of the apparatus, and in the principles of electric currents used in the production of the *x*-rays. This will include also the dangers in their application, their effects upon healthy and diseased tissues, and the methods of protection to the patient and operator. Instruction in the technique of radiographic exposures and the development of plates in the dark room. The therapeutic application of *x*-rays, with technique required for treating various pathological conditions, with demonstrations by treatment of patients. The therapeutic use of Finsen rays and "High Frequency Currents."

6. Orthopedic Surgery. Orthopedic Clinic, Dr. Willard, Tuesdays, 12 to 1; Drs. Young, Spellissy, and Reed, Mondays, Thursdays, and Fridays, 12 to 1; Operations, Lectures, Demonstrations, and Practical Work in the Orthopedic Ward and Dispensary. The Special Orthopedic Gymnasium for the Treatment of Paralyses, Deformities, Curvatures, etc., is open daily from 12 to 2.

7. Pediatric Surgery. Dr. Jopson. Wednesdays and Saturdays, Children's Hospital, 11 A.M. to 1 P.M.

8. Genitourinary Diseases. Drs. Neilson and Siter. In the Out-patient Department of the University Hospital, Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1. This course is altogether practical, and covers the following subjects: Venereal Diseases, Surgical Diseases of the Genitourinary Organs, the Use of Instruments for Diagnosis and Treatment of Diseases of the Urethra and Bladder, and demonstration of operative procedures.

9. Minor Surgery. Dr. Norris, University Hospital, daily from 12 to 1 P.M.

GYNECOLOGY

1. Gynecological Clinic. Dr. Clark. Wednesdays and Fridays, 2 to 4 P.M., University Hospital. The practical work in this course will be limited to five graduate students.

2. Gynecological Clinic. Dr. Beyea Tuesdays and Thursdays, 11 A.M. to 1 P.M., Gynecean Hospital.

3. Gynecological Pathology Dr. Anspach. Hours to be arranged for the convenience of those taking the course. (Limited to ten.)

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Dr. Hirst and assistants. Tuesdays and Thursdays, 3 to 4 P.M., in the Maternity Pavilion of the University Hospital. This course consists in demonstrations of the Surgical Treatment of the Injuries of Childbirth by Primary, Intermediate, and Secondary Operations; Treatment of the Pelvic and Abdominal Complications of the Child-bearing Process by Pelvic and Abdominal Surgery; the Obstetrical Operations, Obstetrical Diagnosis, and Preliminary Examination of the Patient, and the Management of the Puerperium.

DERMATOLOGY

Dr. Hartzell. Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1 P.M. This course is given in the Out-patient Department of the University Hospital and Wards of the Philadelphia Hospital, and will be devoted to the Examination, Diagnosis, and Treatment of patients in daily attendance at the clinic.

NEUROLOGY AND PSYCHIATRY

1. Clinics. Dr. Mills on Mondays and Dr. Spiller on Tuesdays and Thursdays, 3 P.M., at the University or the Philadelphia Hospital.

2. Neuropathology. Dr. Spiller will give practical instruction either by the lantern or in the laboratory once a week for those desiring to take Neuropathology in connection with the clinical work.

3. Electrotherapeutics and Ward Class Demonstrations. At least once a week, by Dr. Potts and assistants, University Hospital.

4. Psychiatry. Dr. Burr. Instruction in Mental Diseases either by lectures or by ward class demonstrations, Wednesdays and Fridays, 3 P.M., Philadelphia Hospital.

5. Special Course. The course announced above is open to all students of the post-graduate department. Any student wishing to take Neurology and Psychiatry as a special subject, or in combination with one or two other subjects, can make arrangements with the Dean of the Faculty and the Teachers in the Neurological Department for the fuller course.

OPHTHALMOLOGY.

This course is designed for those who are especially interested in the eye, and is limited to ten.

1. Operative Clinic. Dr. de Schweinitz, Thursday, 3 to 4 P.M., University Hospital.

2. External Diseases of the Eye, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 3 to 4 P.M.

3. Operations on Animals' Eyes, Dr. de Schweinitz, assisted by Dr. Mellor, Tuesdays, 4.30 to 5.30 P.M.

4. Functional Testing of the Eye, including the principles of Refraction, Muscle-balance Testing, Retinoscopy, and Ophthalmometry. Dr. Carpenter, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 2 to 3 P.M.

5. Pathological Histology. Dr. Shumway, Mondays, Wednesdays, and Fridays, 4 to 6 P.M.

OTOLOGY.

Dr. Randall. (*a*) Daily Clinics at the University Hospital. (*b*) Instruction in the Anatomy of the Ear by means of lantern demonstrations and anatomical preparations in connection with the Wistar Museum of Anatomy.

In demonstrating operative procedures, it is expected that either clinical material or cadavers will be used

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Dr. Grayson. Daily in the Laryngological Clinic of the University Hospital, at 2.30 P.M. A course in Instrumental Technique and in the Diagnosis and Treatment of Diseases of the Nose and Throat. The microscope will be used to supplement the clinical diagnosis of neoplasms and exudative inflammations, and in the treatment. Instruction will be given in the ordinary methods of local therapeusis, but opportunities will be offered to perform the various operations for deflection of the nasal septum, for the removal of polyps, the faucial tonsils, adenoid growths, etc.

Note.—Those desiring to take the course in both Otology and Laryngology may take these subjects on alternate days.

BACTERIOLOGY AND HYGIENE

1. Elementary Bacteriology. Drs. Gildersleeve, daily, 9 to 11 A.M., in the Laboratory of Hygiene. This course is designed to supply the needs of the practitioner of medicine. It comprehends the preparation of culture media, the methods of sterilization, the methods of isolation and study of bacteria in pure culture, the study of the best known and most important of the pathogenic species, the methods of disinfection, the use of the microscope, and the methods of staining employed in bacteriological work.

2. Advanced Work in Bacteriology. Dr. Bergey, daily, 9 to 11 A.M., in the Laboratory of Hygiene. This course will be arranged in accordance with the qualifications and inclinations of each individual student.

3. Practical Hygiene. Dr. Bergey, 9 to 11 A.M., daily, in the Laboratory of Hygiene. Applicants for the course must possess a working knowledge of quantitative chemical analysis. The course covers exercises in the physical and chemical study of the atmosphere, with methods of recording results; studies in ventilation and heating, and methods for estimating extent of the same; physical, chemical, and bacteriological study of water; the artificial and natural methods of water purification; pollutions to which water is liable; interpretation of results of analysis; studies of milk from the sanitary standpoint; sanitary food inspection and analysis.

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2. Toxicology. Tuesdays and Thursdays, 9 to 11 A.M., Robert Hare Chemical Laboratory.

3. Elementary Physiological Chemistry. This course will consist of a systematic study of the carbohydrates, fats, proteids; salivary, gastric, and pancreatic digestions, and of the bile, milk, and blood. If desired, work will be given in tissue chemistry and in general food analysis. (This course will only be given in the event of there being at least six students.)

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UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

THE PELVIC FASCIA AND ITS WHITE LINES.

By George A. Piersol, M.D.,
Professor of Anatomy, University of Pennsylvania.

The universally conceded importance of the pelvic fascia renders it desirable that the contradictions in the current descriptions of this structure shall be reconciled. The influence of the Basel nomenclature (BNA) now adopted by German writers is already apparent in recent text-books in English. That this influence will become more pronounced is certain, although the desirability of consistently adopting the newer terminology in its too often cumbersome Latin form is questionable. Mere exchange of names, however, is a matter of secondary consequence. The real interest lies in the anatomical relations implied. If changes in terminology mark an advance in the clearness and accuracy of conceptions of anatomical relations, recognition of such advances is desirable.

A case in point is the pelvic fascia, in the description of which English and German anatomists differ not a little. In order to appreciate these differences reference to the actual details may be made with advantage.

On viewing the pelvic cavity from above, after removal of the peritoneum, subserous tissue, and vessels, the entire inner surface of this space, except a crescentic area on the anterior wall behind the pubic bones and symphysis and where pierced by organs that pass beyond, is lined by fascia. At the sides the latter is attached to the posterior half of the pelvic brim, behind to the sacrum and coccyx, while anteriorly it leaves the iliopectineal line and gradually descends until, in front, it sinks almost to the line of the lower border of the symphysis. Examined with regard to the muscular structures upon which it rests, above the fascia is seen to cover at the sides the inner surface of the upper part of the obturator internus muscles and, farther backward, the pyriformis muscles. Below, the fascia passes uninterruptedly over the muscles of the pelvic floor, the levatores ani and the coccygei, that are so appropriately designated as the *pelvic diaphragm*. It is evident that, disregarding the interval in the subpubic angle closed by the triangular ligament, the fascia forms a fibrous investment of the cavity of the true pelvis, complete and unbroken except where perforated by the urethra (vagina), rectum, the obturator vessels and nerve, and the branches of the internal iliac vessels.

Notwithstanding the practical continuity of this fascial lining as a continuous sheet, it is usual to apply distinct names to its different portions. That above the origin of the pelvic diaphragm is known as the parietal or pelvic fascia; that covering the pyriformis muscle as the fascia of the pyriformis; while that covering the levator ani and the coccygeus is termed the rectovesical, visceral, or, as designated by the new nomenclature, fascia diaphragmatis pelvis superior. If distinction must be made, although there seems little necessity, the terms *parietal* and *diaphragmatic* are the most appropriate, being convenient and expressing relations. "Visceral" as applied to the fascial covering of the pelvic diaphragm, although convenient and adopted by Luschka and others, and emphasized by Cunningham, is not exact, since throughout the greater part of its extent the fascia has little directly to do with the organs of the pelvic floor and, even below the level of such connections, continues as the specific covering of the levator ani. "Rectovesical" is misleading and should be abandoned.

But why multiply names for what constitutes a continuous sheet? The most appropriate designation for this sheet, it seems to the writer, is that suggested by Merkel, who applies the term *fascia endopelvina* to the layer in question. Endopelvic at once expresses the relations of the fascial lining of the pelvic cavity and removes the perplexing and undesirable subdivision.

The chief objection is that the same name, fascia endopelvina, has been applied by the Basel Commission to the visceral extensions of this fascia on to the organs of the pelvic floor. This restricted use of the term seems unfortunate, since the endopelvic relation of the fascia is true of its general expanse even more than to the limited visceral extensions. The latter are more appropriately spoken of as the *visceral reflections* of the endopelvic fascia.

In the descriptions followed by German anatomists, the obturator fascia is regarded as covering the entire median surface of the obturator internus muscle and, therefore, as approaching the pelvic brim where the muscle reaches almost to the iliopectineal line. Further, they regard the upper part of the obturator fascia as distinct from the pelvic fascia (the supradiaphragmatic portion of the endopelvic fascia), which is consequently described as a thin but separate sheet lying upon the obturator fascia.

That the entire inner surface of the obturator internus is covered by a fascial envelope is, of course, evident, but neither careful dissection of the fresh pelvis nor study of sections of the formalin-hardened structures convinces one of the presence of two distinct fascial layers over the upper

part of the obturator internus. Reference to Fig. 1, *j*, from a frontal section of a formalin body, shows the muscle covered by and attached to a single robust fascial layer that admits of no further separation. The subdivision of this portion of the pelvic lining is unwarranted and the upper segment of the obturator internus is most appropriately described as covered by the supradiaphragmatic part of the endopelvic fascia. The term obturator fascia should be restricted, as it is by English anatomists, to the investment of the muscle below the pelvic diaphragm where it forms the outer wall of the ischiorectal fossa.

On pulling the bladder strongly backward and laterally on the opposite side the endopelvic fascia is seen to present a thickening that appears as a whitish band (Fig. 2, *d*) pelvic and vesical walls. In the male the reflections to the bladder are secondary extensions of the direct connections established by the puboprostatic bands.

Although the tendinous arch is the "while line" par excellence, it differs materially in its relations and significance from the fascial thickening usually described under that name by English and American anatomists, by whom the "white line" is said to correspond to (*a*) the line along which the rectovesical or visceral layer leaves the parietal layer, and (*b*) the fascial origin of the levator ani muscle—two relations which are inseparable.

That the lower tendinous arch, however, has nothing to do with either is shown by both the fresh pelvis and, still better, frontal sections of the hardened structures (Fig. 1, *d*).

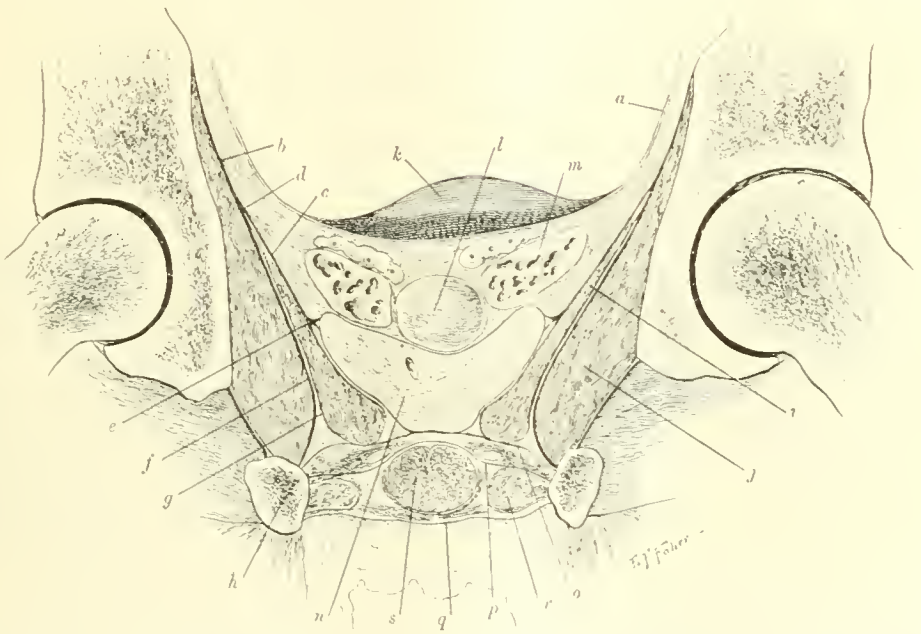


Fig. 1.—Oblique frontal section of male pelvis, passing just anterior to the rectum: *a*, peritoneum; *b*, endopelvic fascia, supradiaphragmatic portion; *c*, diaphragmatic portion of same; *d*, upper white line—fascial origin of levator ani; *e*, lower white line, from which visceral reflections pass to the prostate; *f*, obturator fascia; *g*, anal fascia; *h*, ischial ramus, cut; *i*, levator ani; *j*, obturator internus; *k*, bladder, upper surface; *l*, part of rectovesical layer of fascia; *m*, seminal vesicle; *n*, prostate, cut obliquely; *o*, *p*, superior and inferior layers of triangular ligament; *q*, Colles' fascia; *r*, *s*, crus and bulb of penis.

which stretches from the ischial spine forward and downward to be attached to the posterior surface of the pubic bone near its lower border, at the side of the symphysis. This band, gently curved with the convexity directed outward, is broadest and most distinct from 1.5 to 2 cm. behind its anterior attachment. It sends glistening fibres medially toward the adjacent prostate and bladder, while other fibres radiate laterally and upward into the endopelvic fascia. The thickening in question marks the origin of the visceral reflections and constitutes the *lower tendinous arch* (*arcus tendineus fasciae pelvis* of the BNA). In the female subject, in which the relations are simpler on account of absence of the prostate, the anterior extremity of the arch is continuous with a distinct band, the pubovesical ligament or anterior true ligament of the bladder, that connects the

From these it will be seen that the origin of the muscle, and consequently that of the fascia covering its upper surface, lies higher and is separated from the arcus tendineus by an interval of varying breadth, depending upon the level at which the levator ani arises.

Inspection of the pelvis also shows (Fig. 2, *e*) that the fascial origin of this muscle corresponds to a second, but much less distinctly marked, light band that sweeps, with its convexity directed downward, from the ischial spine toward the anterior margin of the obturator canal. Behind, where both spring from the spine of the ischium, the upper (*arcus tendineus musculi levatoris ani* of the BNA) and the lower (*arcus tendineus fasciae pelvis*) white lines blend, but in front the upper ascends while the lower passes to its attachment near the inferior border of the symphysis pubis.

This differentiation is noted by Thane in his account of the rectovesical fascia in *Quain's Anatomy*, but usually is ignored in the descriptions in our text-books, in many of which the anterior extremity of the inferior arch is confused with the line of origin of the levator ani.

The investigations of Henle, Kollmann, Lartschneider, Holl, and others have established the composite nature of the muscular sheet that in human anatomy is commonly termed the levator ani. As well known, the latter represents muscles belonging to the caudal segment of the spine that even in the tailed apes retain their character as tail-flexors. With the disappearance of the caudal appendage and the assumption of the erect position these muscles take up the important duty of closing the pelvic outlet and, with the coccygeus, become the pelvic diaphragm. Even in their modified condition in man, evidences of the original distinct

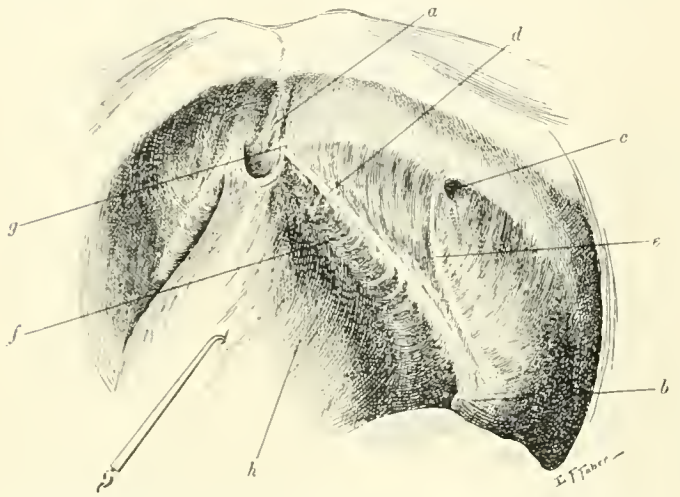


Fig. 2.—Pelvis of female subject viewed from above and the left; the bladder has been drawn backward and to the left to show relation of upper and lower white lines of endopelvic fascia after removal of peritoneum and other overlying structures: *a*, symphysis; *b*, ischial spine; *c*, obturator canal; *d*, lower and *e* upper tendinous arches or white lines; *f*, visceral reflections of endopelvic fascia; *g*, pubovesical ligament; *h*, bladder.

components exist and there are abundant morphological grounds to warrant the subdivision of the levator ani into an iliococcygeus and a pubococcygeus, as adopted by some human anatomists.

As with other structures that have undergone regression, the degree to which the component parts of the levator ani are developed varies and, hence, marked differences are observed in the extent and character of its origin. The variations in the origin of the anterior part of the muscle are pronounced, in some cases the muscles arising almost, if not quite, as high as the level of the obturator canal; in others its attachment to the pelvic wall sinks nearly to the lower tendinous arch, in which case the diaphragmatic portion of the endopelvic fascia is correspondingly reduced. Again, the fibres of origin may be so tendinous that they are not readily distinguished from the fascia, and the muscle apparently springs from a lower level than is really the case.

The chief significance of the lower white line, as the inferior tendinous arch may be called, is as indicating the line along which the visceral reflections of the endopelvic fascia are given off. Anteriorly the lower white line is continuous with the puboprostatic (pubovesical) ligaments between which is a median depression (Fig. 2) closed below by a reflection of fascia. This recess is the bottom of the prevesical space and is filled with the loose retropubic fatty tissue. Behind the pubovesical ligament the tendinous arch marks the origin of fascial expansions that pass to the sides of the bladder (vagina) and rectum.

An interesting view of the relations of these visceral reflections is seen in Fig. 3, drawn from a horizontal section of a female pelvis, the plane of section having passed just

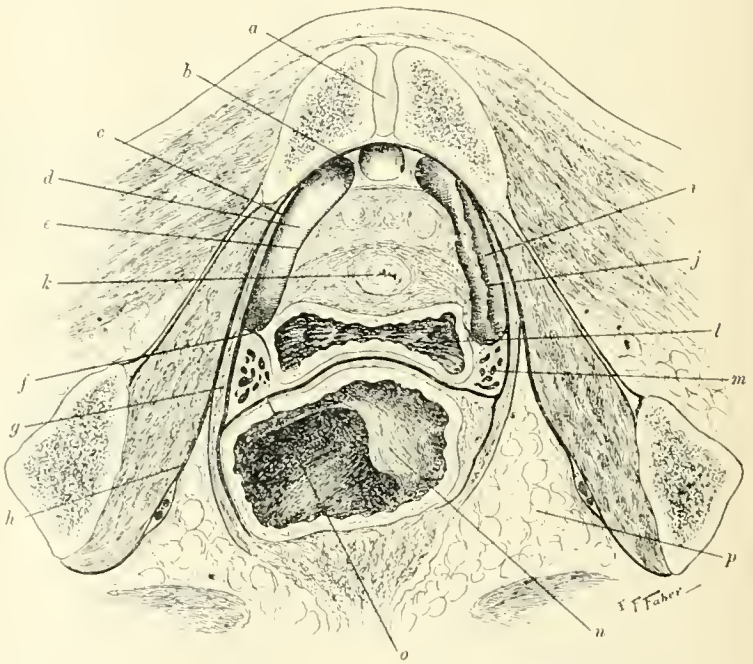


Fig. 3. Upper surface of horizontal section of female pelvis, passing immediately below the bladder: *a*, symphysis; *b*, pubovesical ligament; *c*, endopelvic fascia; *d*, visceral reflection of the latter, forming floor of space filled with fat which has been removed; *e*, reflection of fascia passing to bladder; *f*, same to vagina; *g*, levator ani; *h*, obturator fascia covering obturator internus; *i*, continuation of endopelvic fascia over levator ani; *j*, cut edge of visceral reflection; *k*, urethra; *l*, vagina; *m*, vesicovaginal veins; *n*, rectum; *o*, rectovaginal layer of fascia; *p*, ischiorectal fossa

below the bladder. The loose intervening fatty tissue having been removed, the endopelvic fascia and its visceral expansion are seen as distinct sheets separated by a crescentic groove (*a*), closed below by the lower tendinous arch. On one side (Fig. 3, *j*) the line of reflection of the visceral expansion has been cut through, thus permitting the continuation of the endopelvic fascia to be traced downward over the pelvic diaphragm (levator ani). From the expansions covering the lateral surface of the vagina and rectum,

transverse partitions pass in front and behind the vagina, constituting the vesicovaginal and the rectovaginal septa respectively. In the frontal section of the male pelvis (Fig. 1), the plane of which has passed just anterior to the rectum, a portion of the intervening fascial septum (*l*) is shown. It is to this layer, a part of the visceral reflections, that the name rectovesical is appropriately applied. Its application to the diaphragmatic portion of the endopelvic fascia should certainly be discarded in the interest of accuracy. On the other hand, it seems to the writer, the Germans have gone too far and added needless complexity in designating the visceral reflections as the vesical, prostate, and rectal fasciæ. As to the thin sheet covering the under surface of the pelvic diaphragm, there seems to be no compensating advantage in the substitution of newer names. Although *fascia diaphragmatis pelvis inferior* (BNA) expresses definite anatomical relations, and, therefore, theoretically is desirable, it is doubtful whether this cumbersome term will supplant the convenient name (anal fascia) now in use.

A COMPARISON OF THE AGGLUTINATING PROPERTIES OF THE SERUM OF TYPHOID FEVER PATIENTS ON THE B. TYPHOSUS, B. ENTERITIDIS (GAERTNER), AND B. PARATYPHOSUS (A.), AND THE RELATION OF THEIR INDIVIDUAL ANTISERA.

By Herbert Fox, M.D.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

During the year 1904 the sera that were sent to the Pepper Laboratory from the University Hospital for Widal tests were tried with the three organisms mentioned in the title of this contribution. In all there were 148 cases, of which 94 were true typhoid fever. The dilution used for diagnostic purposes was 1:50, but for scientific examination 1:500 was employed. The cultures (twenty-four hours in peptone broth) were always filtered through a close paper in order to obtain a small number of micro-organisms and establish a control that was without clumps or in which spontaneous segregation could be observed.

The spontaneous clumping of these germs deserves some mention. The organisms arranged themselves perpendicularly or parallel when such uninfluenced action occurred in controls of B. enteritidis. These clumps varied in size as spontaneous clumps of any other bacterium, but the rectangular arrangement seems peculiarly single and is not difficult to recognize. The voluntary segregations of the B. typhosus and B. paratyphosus did not display this regular distribution and resemble the active ones.

Also in the active or forced clumping of these bacteria the Gaertner bacillus stands alone. The clumps of this organism are compact and quite rarely contain moving elements. The other two species give rise to clumps which are loosely interwoven at many angles and may contain one or more moving individuals. Large clumps of the B. typhosus and paratyphosus appear wavy and streaked, while corresponding masses of the meat poisoner are finely grained. This last observation may be explained on the ground that the flagella are probably fewer and shorter on this meat-poisoning bacillus, thereby allowing closer approximation of the single cells. This is, however, by no means always true of these species.

These differences are not marked enough to be diagnostic, and are only noticeable when several comparative tests are made.

The Action of Typhoid Serum with B. typhosus and B. paratyphosus. Only 12 of the 94 sera of the clinical enteric fever cases showed any agglutination of the paratyphoid organism. Four of these 12 cases were proven to be true typhoids by blood culture, the entire 12 cases giving diagnostic reactions with the B. typhosus.

Cases No. 56 (typhosus 250, paratyphosus 50), No. 59 (typhosus 250, paratyphosus 50), No. 66 (typhosus 50, paratyphosus 50), No. 86 (typhosus 250, paratyphosus 50), No. 111 (typhosus 50, paratyphosus 50), and No. 117 (typhosus 500, paratyphosus 50), it will be seen, reacted only as high as 1:50, while cases No. 33 (typhosus 250, paratyphosus 250) and No. 169 (typhosus 250, paratyphosus 250) reacted at a dilution of 1:250. The serum potency reached 1:500 in cases No. 78 (typhosus 500, paratyphosus 500), No. 123 (typhosus 500, paratyphosus 500), and No. 137 (typhosus 500, paratyphosus 500). In only 1 case (from which the typhoid bacillus was obtained in the blood) was the dilution for the paratyphoid higher than for the typhoid bacillus. Chart I. gives the dilution limits for these 12 cases, and case No. 179 will show the exception. Chart II. gives the curve for this case. This was a prolonged typical attack of enteric fever, and a blood culture was taken because of the marked paratyphoid reaction. As stated above, only the B. typhosus in pure culture was found. The patient was a private one and, the results being considered final, no further study was allowed. That this was a mixed infection may be surmised, especially when we take into consideration the low percentage of paratyphoid reactions in true typhoid fever, but such an opinion may not be made positively. The cases in this series which were

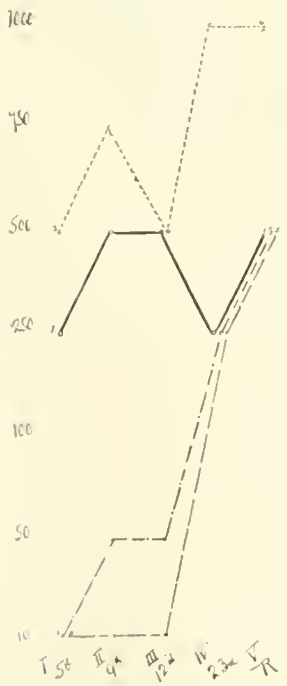
proven typhoids are No. 78 (typhosus 500, paratyphosus 500), No. 86 (typhosus 250, paratyphosus 50), No. 117 (typhosus 500, paratyphosus 50), and No. 179 (typhosus 500, paratyphosus 1000). It will be seen that in 6 cases these two organisms were clumped to the same limit, while in 5 the typhoid bacillus was affected in higher dilutions, and in only 1 case was the reverse true.

Chart I.—Positive Paratyphoid Reactions.

		Typhoid Bacillus.							Paratyphoid "A"						
No.	Day.	10	50	100	250	500	750	1000	10	50	100	250	500	750	1000
33	?	+	+	+	+	+			+	+	+	+			
56	4	+	+	+	+				+	+					
59	12	+	+	+	+				+	+					
66	6	+	+						+	+					
T. F., 78	9	+	+	+	+	+			+	+	+	+	+		
T. F., 86	?	−	+	+	+				−	+					
111	8	−	+						+	+					
T. F., 117	12	−	+	+	−	+			+	+					
123	8	+	+	+	+	+			+	+	+	+	+		
137	?	— + +	+	+	+	+			+ + +	+ +	+	+	+		
169	11	+	+	+	+				+	+	+	+			
T. F., 179	5	+	+	+	+				+	+	+	+	+		
	9	+	+	+	+	+			−	+	+	+	+	+	
(Vide Chart No. 2)	12	−	+	−	−	−			+	−	+	+			
	23	−	+	+	+				−	+	+	+	+	+	+
	R.	+	+	+	+	+			+	+	+	+	+	+	+

R. indicates relapse.

Chart II.—Case 179. True Typhoid Fever.



Curve for B. paratyphosus "A" – – – – –(2)
Curve for B. typhosus ————————(1)
Curve for B. enteritidis — — — —
Curve for B. paracolon or paratyphoid "B" — . — . — .

The Action of Sera of Animals Immunized Against B. typhosus and B. paratyphosus. The animals were inoculated in the usual manner, injections being made every eight days and bleedings done two days after the second, fourth, and seventh injections. This time of bleeding was adopted to obtain the agglutinating body produced by the first, third, and sixth injections respectively, because at that time, ten days after the injection, it has about reached its climax, and passed the temporary diminution following the immediately preceding injection, and probably called into greater activity by this immediately previous inoculation. The serum of the rabbits immunized against B. typhosus had no effect upon B. paratyphosus except in one rabbit; when the serum had a homologous potency of 1:10,000 a reaction of 1:10 was observed. The serum of the animal inoculated with B. paratyphosus clumped the typhoid bacillus, in dilution of 1:10, throughout the process of immunization—that is, at all three bleedings. The limit for the latter remained the same whether the potency for the former was 1:10 or 1:5000, as was the case at the last bleeding.

Furthermore, the writer has had for over a year four samples of Parke, Davis & Co.'s antityphoid serum; this clumped the B. typhosus to very high limits, but had no effect whatever on the B. paratyphosus.

The Action of Typhoid Serum with B. typhosus and B. enteritidis. Of the 94 cases of clinical enteric fever, 82 (87 per cent.) gave a positive reaction with the B. enteritidis (Gaertner) at some time or other during their course. This fact has been known for a long time, but the precedence of the reaction was the point for solution. Nineteen of these 82 cases were tested more than once, and 14 of these 19 gave a reaction to the Gaertner bacillus which appeared before the reaction to the B. typhosus, or was obtainable in higher dilutions. (Chart III.)

Chart III.—Cases with High Value for Bacillus Enteritidis.

Case No.	Occasion and day of disease.	B. typhosus.				B. enteritidis.			
		1:10	1:50	1:250	1:500	1:10	1:50	1:250	1:500
21	1st-8th	+				+	+	+	+
	3d-25th	+	+	+	+	+	+	+	—
50	1st (?)	—				+	+	+	+
	2d (?)	+	+			+	+	+	—
83	1st (?)	+	—				+	—	
	2d (?)	+	+	+	+	+	+	+	+
58	1st, 2d	+	+	+	—	+	+	—	
	2d-9th	+	+	+	+	+	+	—	
89	1st-4th	+	—		+	+	+	+	+
	2d-11th	+	+	—		+	+		
91	1st-9th	—				+	+	+	+
	2d-15th	+	+	+	—	+	+	—	
116	1st-8th	—				+	+	+	—
	2d-14th	+	+	+	+	+	+	—	
124	1st-7th	—				+	+	—	
	2d-10th	+	+	+	+	+	+	+	+
126	1st-8th	+	—			+	+	+	—
	2d-11th	+	+	+	—	+	+	—	
137	1st (?)	—				+	+	+	+
	2d (?)	+	+	+	+	+	+	—	
	3d (?)	+	+	+	—	+	+	—	
198	1st-9th	—				+	+	+	+
	2d-20th	+	+	+	+	+	+	—	
127	1st-6th	—				+	+	+	+
	2d-13th	+	+	—		+	+	—	
199	1st-8th	—				+	+	+	+
	2d-15th	+	+	+	+	+	+	+	+
200	1st-13th	—				+	+	+	+
	2d-21th	+	+	—		+	+	—	

Especially is this marked in cases Nos. 21, 50, 89, 91, 116, 127, 137, 198, 199, and 200. De Nobele noted in animal

experiments that the typhosus agglutinins disappeared more slowly after an infection than did the enteritidis agglutinins. If we examine the limits of dilution in 70 cases of typhoid fever, for these two organisms according to first, second, and third week of this disease, we will find an analogous curve. The remaining 12 cases are so indefinite in their history as to nullify attempts to date them, even approximately: 24 cases first week, limit for B. typhosus 222, B. Gaertner, 325; 43 cases second week, limit for B. typhosus 275, B. Gaertner 260; 3 cases third week, limit for B. typhosus 500, B. Gaertner 175.

Among those 14 cases examined more than once, 9 (64 per cent.) exhibited a superior potency for the meat poisoner at the first examination, followed by a decline of this value and a corresponding rise in the limit of dilution for the B. typhosus. In the five exceptions to this the limits at the first and subsequent examinations were practically the same. This seems to indicate that agglutination of the enteritidis appears early and disappears likewise early, while the special clumping body of the B. typhosus appears somewhat later and persists for a longer time than the substance which affects the coagglutinated bacterium.

Additional proof of this is given by a study of sera of animals immunized against these bacilli. The antityphoid serum at the first examination—*i. e.*, after the second inoculation—clumped the B. enteritidis much more highly than the homologous species, but at the second test the dilution limits were the same for both. At the third trial the limit for the meat poisoner had remained as before, while that for the typhoid bacillus had forged ahead, in one rabbit fivefold, in another tenfold.

The previously mentioned therapeutic serum agglutinated the B. enteritidis to about a half the limit of the typhoid organism. In the microscopic preparations of the lower dilutions of these tests, small swellings and depressions of their envelopes could be discerned in single cells of both species. These grew, upon standing, into clear spaces within the capsules, which, on examination with the oil immersion, appeared finely granular. This was probably a lysogenic process. This distortion and vacuolization was not observed in the tests with the B. paratyphosus and this serum, nor during the experimental immunization by the writer.

The serum of the anti-Gaertner rabbit possessed the same value at first for the B. enteritidis and typhosus. At the second bleeding the homologous bacillus was agglutinated twice as highly as the coagglutinated species, while at the third test this serum contained ten times the amount of agglutinin for the organism used for injection.

In the 12 cases that showed an agglutination of the B. paratyphosus there was also clumping of the meat poisoner, and since these cases gave a coincident reaction to the B. typhosus, no deductions can be drawn. There was no relationship existing between the relative values of the 12 sera with regard to these species. The antisera of these two organisms showed no mutual interaction above the dilution of 1:10.

As control experiments, 6 samples of normal blood, 8 samples of blood of cases with fermentative diarrhœas of childhood, 4 cases of bloody diarrhœa in adults (in which the dysentery group was supposedly the cause), 3 cases of chronic constipation, 2 cases of gastroenteritis, were tried with all these species. In no one was there a reaction above 1:10.

These studies seem to justify the following conclusions:

1. That only a small proportion (12.5 per cent.) of typhoid-fever sera show an agglutinative effect upon the B. paratyphosus (A.).

2. That a great majority of typhoid fever sera give a concomitant reaction with the B. typhosus and B. enteritidis.

3. That early in the attack the reaction to the meat-poisoning bacillus is greater than to the B. typhosus, and the limit for the former declines as the special reaction to the latter rises during the advancing infection.

4. That the behavior of the agglutinins in typhoid fever blood to all the organisms investigated is essentially the same as in the blood of immunized animals.

5. That the experiments show a close relationship of the agglutinating bodies of the B. typhosus and B. enteritidis, or a similarity in their binding power to certain products of body cells that form these agglutinins.

6. That there is no similarity or relationship in the agglutinins or binding powers of the B. typhosus and paratyphosus (A.), and that the coagglutination of these species may be accounted for by group agglutinins or by previous infection. The possibility of a mixed infection is not entirely nullified.

It has lately been declared by Parke and Collins, who worked on the Shiga group and its serum relations, that the species used for immunization is agglutinated in higher dilutions throughout than a coagglutinated organism is. In these experiments the antityphoid sera clumped the B. enteritidis more strongly at the first test than the homologous organism, while the antienteritidis sera gave as high (or higher) values for the organisms injected as for the B. typhosus. The strains used were all good agglutinators and possessed excellent agglutinogenic power; they were not affected by the rabbit's blood at 1:10 before injections were begun. To explain these results, we may hope for assistance in the mechanism of the production of agglutinins.

The body cells which produce agglutinins, or any other antibodies, cannot be supposed to react immediately to all kinds of chemical matter with which they come into contact, and must therefore be considered as possessing receptors of simple nature. The simple receptors become specialized after having been once attacked by a certain influence, and

we can safely assume that thereafter they would only react to the same stimulus or one akin to it. The general receptors that have not become specialized, but which have increased their activity because of the distraction of specialized receptors, might therefore have a greater influence than normally upon these kindred but not identical stimuli.

To apply this to the foregoing experiments we may consider antityphoid sera as reacting to the B. typhosus because the stimulus is homologous, and as reacting to B. of Gaertner because the stimulus of this species is similar; therefore, it may be said that an agglutinating serum contains a special agglutinin to the injected organism, and an indefinite amount of normal agglutinin. The special agglutinin is composed of some elements which are truly specific, and other elements which find a mutual activity with a heterologous bacterium. Now, assuming that the non-specific elements act upon their mutual elements in the heterologous bacterium, aided by the probably increased activity of the normal agglutinins, the result would probably be greater with this bacterium than with the homologous species early in the infection. Before the bonds of union between the individual components of the specific and shared portions in the special serum had become firm, the binding power of the shared or common elements might be greater for the heterologous bacterium. Later, however, the bonds of union of the integral parts of the special serum may have become so firm that the weaker binding power of the coagglutinating bacterial elements cannot attract any combination with their mutual relations in the shared portion of this special serum; therefore, it may be that the high dilutions that clumped the B. Gaertner at the first bleeding of the antityphoid rabbit resulted from a strong avidity of the mutual elements of the antityphoid serum and the meat-poisoning bacillus, aided by activity on the part of the non-specialized normal agglutinin. (Indeed, in three controls from cases in which none of these organisms could have been active, a 1:10 reaction with the B. Gaertner was noted.) Later, however, the value of the serum for the meat poisoner did not increase, because the constituents of the special antityphoid serum were firmly combined and reacted more strongly to the homologous elements of their bacteria.

On the other hand, to explain why the anti-Gaertner serum clumped itself as high or higher than the B. typhosus, we must assume that the binding power of the common elements in this special serum and in the typhoid bacteria was less than the strength of the bonds of union between all the elements of the special serum.

Antityphoid serum will behave with the B. coli communis as it has in these experiments with the B. enteritidis, and the anticolon serum resembles the anti-Gaertner when tried with the B. typhosus.

The effect of the antityphoid serum on the paratyphoid organism may be limited to the ability of the abnormally active, non-specialized receptors to affect it, while the special receptors find no mutual activity present. Group agglutinations are, therefore, due to kindred combining powers of agglutinin on the one hand and agglutinable body (or agglutinogen) on the other, the difference in dilution necessary for reaction being proportionate to the quantities of their relatively mutual constituents.

The following, for instance, is Durham's hypothesis. He represents, for example, the B. typhosus agglutinin as A+B+C+D+E, and its agglutinogen (agglutinable substance) as a+b+c+d+e. B. of Gaertner agglutinin he indicates as C+D+E+F+G+H, while the bacillary agglutinable body is correspondingly c+d+e+f+g+h. Now, when homologous agglutinin is added to the components of the bacillary agglutinogen, the maximum result occurs. But if the agglutinin and agglutinogen (B. typhosus, A+B+C+D+E)+(B. Gaertner, c+d+e+f+g+h) be not homologous, a partial combination of the elements (c, d, and e) takes place and the limit of the reaction would depend upon the relative amount (in factors?) of those mutual constituents, and their avidity for one another. Possibly the other elements, not susceptible to the employed agglutinin, may be affected by the highly active, non-specialized receptors of the agglutinating serum.

Now, suppose the agglutinogen of another organism be made of e+f+g+h+j+k and its agglutinin be E+F+G+H+J+K (Durham's article, B. of Hatton, and, to modify Durham's argument to apply to these experiments, let us suppose that this formula represents the B. paratyphosus [A.]). The agglutinin of the typhoid bacillus and the agglutinogen of B. paratyphosus (A.), therefore, have only one common element, E.; so that were they combined the strength and concentration of the serum used would have to be so much greater to obtain a result. Furthermore, Durham supposes that any constituent, either of an agglutinin or agglutinable body, is not necessarily in the same quantity as the other constituents, or the same as that particular element would be in another serum or culture. If its amount might vary, so might its chemical combining powers, and the reaction described between heterologous agglutinin and agglutinogen might not occur at all.

The exceptions (twelve) noted in the experiment with typhoid sera and paratyphoid organisms may be explained on the basis that the particular strains of organisms, which were the etiological moment in these twelve cases, gave rise to an agglutinin which contained elements mutual to the strains of paratyphoid organisms used, or that the binding powers of these individual constituents may have been very active.

Another possible explanation of these exceptions is a previous infection (typhocolon, since we are considering them) of the intestines, gall-bladder, or other location, which produced and left in the blood traces of an agglutinin which had individual elements that found a mutual activity in

the elements of the bacillary composition of the paratyphoid strains used for the agglutination tests.

It appears to the writer that the last explanation offers a suggestive solution to those cases giving a high clumping value with a coagglutinated organism.

The theory of partial similarity of two agglutinins or agglutinogens seems to present a more satisfactory explanation for the lower dilution limits of coagglutination.

I wish to express thanks and appreciation for the assistance and advice of D. J. S. Evans and Dr. Stengel in the course of this work.

References.

Durham, Herbert E. Journal of Experimental Medicine, vol. v. p. 353. Journal of Pathology and Bacteriology, 1897, vol. iv. pp. 13 and 388. Ibid., 1901, vol. vii. p. 240.

Horton, Smith. Goulstonian Lectures, Lancet, 1901, vol. i.

Neufeld, F. Handbuch der path. Mikroörganismen, 1902, 6th and 7th parts, p. 279.

Pfeiffer u. Kolle. Zeitschr. f. Hygiene u. Infekkrht., 1896, Bd. xxi., S. 203.

Parke and Collins. Journal of Medical Research, 1904, vol. xii.

Van Ermengen. Handbuch der path. Mikroorganismen, 1902, 9th and 10th parts, p. 652.

Vaughan, V. C., Jr., and Buxton, B. H. Journal of Medical Research, 1904, vol. xii., No. 1, p. 115.

STUDIES TO DETERMINE THE ACCURACY OF THE STANTON BLOOD-PRESSURE APPARATUS.

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In this short communication I wish to describe the methods used by me in determining the accuracy of the Stanton apparatus in registering the maximum and minimum blood pressure, and to give briefly the results obtained.

I am well aware that much of this work has been done before, but I believe the method employed in this series of experiments is slightly different from those already published.

It is not my purpose to review the prolific literature on the subject of blood pressure and the methods of its determination, but simply to describe and give the results of the experiments performed in the Pharmacological Laboratory of the University of Pennsylvania.

The experiments were carried out in two series:

Series 1. A large, healthy dog was etherized, tracheotomy was performed, and a glass tube was placed in the trachea, extending to the bifurcation. The carotid artery was then isolated upon one side, as high up as possible. Into this artery was placed a cannula connected with a U-shaped mercurial manometer. The tubing connecting the cannula with the manometer was filled with a saturated solution of sodium bicarbonate to prevent coagulation. The needle of the manometer was so arranged that it stood at zero on a millimetre scale before the clip was removed from the tubing. Then around the dog's neck, below the cannula, was placed the rubber collar of Stanton's apparatus.

When an observation was to be made the clip was removed from the tubing connecting the cannula with the manometer; the movement of the needle, therefore, would indicate practically the absolute maximum and minimum pressure in the arterial system, allowing for a slight error caused by the inertia of the mercurial column.

After this the Stanton apparatus was inflated until the pulsation of the needle of the manometer ceased, the finger was then placed upon the artery directly, and the air was let out of the Stanton collar until a slight, but distinct, pulsation was felt by the finger. It was noted that pulsation was seen in the mercurial column of the manometer some seconds before the pulsation of the artery could be felt. The height of the column in the Stanton apparatus was read now as indicating the maximum pressure and at the same moment the maximum rise of the pulsation needle of the manometer was also read. It is evident that as the manometer was a U-shaped one, all the readings must be doubled. The minimum pressure was determined in the Stanton apparatus by allowing the air to pass out of the inflated collar until we obtained the greatest variation of the mercurial column.

The minimum reading of the manometer needle was compared with this. It is perfectly evident that the constriction of both carotid arteries must cause a rise in the general arterial pressure. It was, therefore, very important that both the observations be made at the same moment. Table I. will show the result of these experiments. It will be noted that there were nine maximum observations and seven minimum observations. This table represents three different animals. In the maximum observations two are the same, in two the Stanton is 5 millimetres lower, and in three the Stanton is 10 millimetres lower. In the minimum observations one is the same, in one there is no arterial observation to compare, and in five the Stanton is 10 millimetres higher. In many of the readings there were three observers to determine the point at which the mercurial column in the Stanton apparatus had the greatest variation; there were always at least two observers and sometimes three; in determining the moment of the return of pulsation in the artery there was one or two observers. By this method, then, we can conclude that the average maximum

error is $6\frac{2}{3}$ millimetres and that the average minimum error is 5 millimetres.

Table I.—Absolute Pressure taken in Carotid.

Artery.		Collar.	
Maximum.	Minimum.	Maximum.	Minimum.
180	130	180	140
180	150	170	140
190	160	180	170
200	140	190	150
200		195	
180	160	175	160
110		120	90
130	110	140	120
160		160	

The greatest variation in the maximum is 10 millimetres, but this may be either plus or minus. In the minimum observations the greatest variation is 10 millimetres and this is always in favor of the Stanton.

After studying the possible errors in this method I came to the conclusion that the partially constricted vessel when the maximum observation was taken did not of necessity represent with absolute accuracy the true arterial pressure.

The question arose how to avoid this difficulty. Some previous experimenters had disseeted out, completely, one carotid artery and the trachea, and had passed a small collar made for the purpose underneath these two structures and then arranged the apparatus practically as I had done. Such a method, however, involves a change in the size of the apparatus together with some constriction of the vessel as it is stretched over the collar, both of which are sources of error. Finally, I decided to take the absolute pressure from the femoral artery, the collar being arranged as before. In the neck the skin was incised, high up over the carotid, so that the pulsation could be easily felt.

Before the adoption of this method, however, it was necessary to determine the differences in pressure in the femoral and carotid vessels. By actual experimentation with two manometers I determined that the average carotid maximum pressure was about 20 millimetres higher than that of the femoral, while the minimum pressure in both vessels was practically the same. Dr. E. T. Reichert informs me that this is approximately correct.

Therefore, in the second table of experiments, which includes thirty observations on different animals, with markedly different conditions of pressure, low pressure being obtained by bleeding the animals, and the high by the use of cardiac and vasomotor stimulants, such as digitalis, 20 millimetres have been added to the maximum pressure as attained in the femoral artery. From an examination of Table II. it will be seen that five maximums tally exactly, in thirteen the carotid artery is above the collar maximum, and in the remainder below. The greatest variation in the maximum records is in two instances where the pressure was so low it was impossible to obtain a minimum pressure with the collar. Here the variation was 50 to 45 millimetres. Excepting these two examples the greatest variation in the maximum is 20 millimetres and in a number of instances it is only five.

Table II.—Absolute Pressure taken in Femoral.

Twenty millimetres added to each maximum artery observation; minimums practically the same.

Artery.		Collar.	
Maximum.	Minimum.	Maximum.	Minimum.
150	80	155	85
130	100	150	90
144	90	140	80
90	60	90	85
110	80	95	80
90	68	80	70
120	80	105	80
120	80	110	80
150	100	130	100
150	84	160	115
144	80	150	115
139	80	130	100
130	80	140	85
120	76	125	85
140	70	150	90
130	80	140	85
130	80	145	90
130	80	140	100
220	100	220	120
200	120	190	120
200	100	185	110
220	100	220	120
240	120	230	135
250	140	255	175
220	110	235	120
250	160	250	185
200	140	180	135
110	80	60	
100	60	55	
100	70	120	80

In the minimum observations the Stanton was above the artery in twenty instances, and the greatest variation is 35 millimetres; this occurs twice. In five instances the reading was the same. The greatest variation, where the collar was less than the artery, was 10 millimetres in three instances. The average maximum error is $12\frac{1}{6}$ millimetres; the average minimum error is 12 millimetres plus.

Conclusions: That though the average errors by both methods seem to be low, yet the variations may be either above or below the Stanton, so that it is impossible to obtain an exact figure to add to, or subtract from, the reading of the Stanton apparatus in order to account for the error. In other words, the amount of error is not constant.

2. That though the average error is low, in single instances the error may be very great, so that for clinical data the blood pressure, both maximum and minimum, should be taken repeatedly to get an approximated idea of the true blood pressure.

A STUDY OF FIFTY CASES OF PERFORATION IN TYPHOID FEVER

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(Concluded from page 89)

SUMMARY OF CASES.

Case I.—J. K., aged twenty-four years, hospital No. 643; admitted May 31, 1901. *Perforation*, *operation*, and *death* on June 12. Admitted on the fourteenth day of typhoid fever, with a high temperature of about 104°, without much reduction from sponging, which was tried for several days. He responded much better to the tubs, and the pulse, which was rapid from the start, became immediately reduced, though the temperature continued high. Occasional delirium was present, and on June 11th, the twenty-fifth day of illness, he complained of general abdominal pain, which increased during the night. At 2 A.M. the following day vomiting of a greenish liquid began; the abdomen became distended, but the liver dulness continued present. No fall in temperature occurred beyond one degree. There was slight abdominal rigidity. Dr. Packard made a diagnosis of probable perforation; operation performed by Dr. Harte at 11 A.M. The leukocytes at 9 A.M. were 3000. On opening the abdomen a perforation in the ileum was found; general peritonitis present. Death five hours after operation.

Case II.—A. A., aged twelve years; hospital No. 983; admitted June 28, 1901. *Typhoid fever, perforation, operation,* and *death* on July 9th. In medical ward on sixth day of typhoid characterized by constipation, with pain in stomach and abdomen. He had some bronchitis, especially in the right side. Fine crepitant rales were heard at the right apex. He had a distressing, hacking cough. The belly was distended, but not tender. For a week after admission the temperature was high, 103° to 104°, without diarrhoea; no hemorrhage. He was delirious. The abdomen was noted to be tympanitic on the thirteenth day. On July 7th, the fifteenth day, the belly became tender in both iliac regions, and the patient had a peritoneal expression. The leukocytes at 8.30 P.M. were 12,440; at 10 P.M. they were 12,430. Perforation was diagnosed by Dr. Packard. Dr. Harte operated at 1 A.M. The peritoneal cavity was full of intestinal contents, and gas escaped. Perforation in ileum discovered one-fourth inch in diameter, near the ileocæcal valve.

He died in the early morning of July 9th, the seventeenth day of his illness.

Temperature. 1.30 P.M. the temperature was 102°; respiration, 32; pulse, 128; 4.30 P.M. the temperature was 102.3°; respirations, 36; pulse, 140; 6 P.M. the temperature was 98.3°; respirations, 32; pulse, 120; 9 P.M. the temperature was 101.2°; respirations, 32; pulse, 120. Fall of 4° (102° to 98°) in two hours, with subsequent reactions.

Case III.—A. J., aged thirty years; hospital No. 1256; Italian; admitted July 10, 1901. *Perforation, operation*, and *death* on July 18th. Admitted to the ward after a two weeks illness characterized by vomiting, diarrhoea, and severe abdominal pain. On admission the belly was generally tender, spleen readily palpable. The urine contained a trace of sugar and showed abundant hyaline and epithelial casts. On July 16th, the fifteenth day of illness, abdominal pain was noted, and on the following day consolidation in the right axilla and the base of the right lung was discovered. Axillary dulness was high in the fifth space. Pain was marked over the abdomen, especially in the left iliac region. By the following morning, the sixteenth day of disease, the belly was rounded, with rigidity present, especially in the upper abdominal zones. The knees and thighs were flexed. Liver dulness present in the sixth and seventh spaces only. Leukocytes at midnight, 5000; at 1.30 A.M., 3840; at 3 P.M., 3000. Hippocratic countenance. Perforative peritonitis diagnosed by Scott, and operation was performed by Le Conte at 11 P.M. In this case the incision was made in the upper right abdominal zone, because great pain and tenderness were present over the gall-bladder. No cholecystitis was present, the appendix was normal, a portion of the ileum was adherent to the abdominal wall, and upon being freed showed a necrotic patch in the long axis of the gut, which seemed about to perforate. General peritonitis; death; no autopsy.

This case is interesting from a diagnostic standpoint, much of the pain being focused over the liver, and was probably due to the pleurisy at the right base. A suspicion, however, of gall-bladder infection in this case was marked; and though actual perforation of the gut was not demonstrated at operation, doubtless the necrotic gut was the cause of some of the abdominal symptoms.

Case IV.—M. G., aged twenty years; hospital No. 1415; admitted July 24, 1901. *Perforation, no operation*, and *death* on August 7th. In medical ward on eighth day of typhoid fever. She had two chills four days before admission, and one the day prior to admission. On this day she had much abdominal pain and began menstruating, which was one week ahead of time. The belly was flat, rather rigid and tender, especially in the left upper zone. The spleen was enlarged, and spots were present. From the beginning the pulse rate was very rapid, running from 112 to 124. High temperature,

104°, not much reduced by sponging; rapid loss of flesh; by August 2d, the seventeenth day of disease, the abdominal distention was noted as troublesome. The temperature was irregular. She sweated at intervals, and was very weak and very toxic. At 8 o'clock on the twentieth day, August 5th, she had a chill. From 8 o'clock on the following morning there was a gradual fall in temperature from 101° to 99°, during which time the pulse also fell from 140 to 108, 92, 88, and 80, while the respiration rose to 32 and 40. At 2 A.M. she had a second chill, with great abdominal pain, tenderness, and rigidity. Perforation was diagnosed by Dr. Henry, but the patient's condition was regarded as hopeless, and no operation suggested. She died the following morning. The temperature had again risen to 106 $\frac{2}{5}$° at 6.30 A.M. No hemorrhage present in this case.

Case V.—S. J., aged twelve years; hospital No. 1436; admitted July 26, 1901. *Perforation*, *operation*, and *death* on July 31. Admitted to medical ward on tenth day of typhoid fever, with bronchitis; the belly was round, slightly distended, and somewhat generally tender on palpation, especially about the umbilicus. The leukocytes were 4900 on the eleventh day. During the night of July 27th to 28th, the twelfth day of disease, the temperature fell from 100° to 98 $\frac{1}{5}$° at 9.15 A.M. The belly was tympanitic; the right rectus was more rigid than the left, though both were tense. The leukocytes at 11.30 A.M. were 7080; at 1 P.M., 5400; at 4.30 P.M., 4950. The pain was mostly centred about the umbilicus. Perforation was diagnosed on the twelfth day, and operation was done by Dr. Stewart at 5 P.M. A pinpoint perforation six inches from the ileocæcal valve was found. The patient died of general peritonitis on the evening of July 31st. Culture from the fluid in abdominal cavity showed bacillus coli and the streptococci pyogenes.

Case VI. P. U., aged eight years; hospital No. 3598; admitted February 1, 1902. *Perforation*, *operation*, and *death* on February 7th. In medical ward on seventh day of illness, characterized by headache and vomiting. Had round, soft abdomen with palpable spleen. Temperature range for one week of 103°. But little reduction under sponging. Pulse was rapid, 124 from his admission; respirations 24 to 28. At 9.30 A.M. on the thirteenth day the belly was noticed to be very tender, slightly distended, and the liver dulness was absent. Perforation was diagnosed by Dr. Scott, but operation was postponed, owing to the delay in securing consent of the parents. Operation at 4 P.M. by Dr. Harte. Perforation found in ileum, with free feces in abdominal cavity; general peritonitis present. Died, after thirty-two hours, with general peritonitis.

In this case nothing in the temperature, pulse, or respiration between 10 A.M. and 1 P.M. showed any change, although the symptoms pointed to perforation about 9.30 A.M.

Case VII.—S. G., aged thirteen years; hospital No. 28; admitted April 4, 1902. *Perforation*, *operation*, *three relapses*, and *recovery*. Discharged August 21st. Admitted to medical ward after eight days illness, with the usual prodromes. Had abdominal pain before admission. Had a severe attack, with high temperature which did not respond well to either sponges or tubbing. On the eleventh day the belly was noted as being tympanitic. An intercurrent relapse, with continuous high fever, began on the twenty-seventh day and continued until the fortieth day, when the fever began to abate. Up to this time he had had one hundred and sixty baths and fourteen sponges. The belly became tender, tympanitic, and distended on May 8th, the forty-second day of disease. Liver dulness was present, however. His condition seemed improved in every way the following day, although the liver dulness was diminished, temperature had fallen to 99, while the leukocytes were 5300. Improvement continued the following day, but early on May 11th, the forty-fifth day, he had a chill followed by an acute rise in temperature, with rapid, feeble pulse. The liver dulness was still present. Dr. Harte, in consultation, advised operation. Eight ounces of free straw-colored fluid were found in the peritoneal cavity, two perforations in the ileum, and the appendix was gangrenous and perforated. The day following operation the patient was pulseless; had vomiting, hiccough, and his condition was considered hopeless. Slight improvement, however, occurred in a few days, and the surgical convalescence was satisfactory. Eighteen days after the operation he had a rise in temperature which was maintained for seventeen days, a second relapse lasting from the sixty-third to the eightieth day of his disease. He became much emaciated. From July 9th to July 21st, the one-hundredth to one-hundred-and-twelfth day, a third rise in temperature occurred, probably a third relapse. From this time, however, his recovery was uneventful.

This is a remarkable case from several standpoints, and emphasizes the fact that apparently hopeless cases will recover after undergoing operation and repeated relapse.

Case VIII.—S. F., aged fourteen years; hospital No. 269; admitted April 26, 1902. *Perforation* and *operation*, with *recovery*. Discharged June 6th. This patient stated that he was in this hospital with typhoid fever of moderate intensity, and was discharged one month before this admission. In looking over the records, however, no record of this admission can be discovered. It is probable he was in another hospital. Two days before admission to the surgical wards he had severe abdominal pain and became very ill. His attending physician diagnosed appendicitis. The boy walked to the receiving ward of the hospital, where he presented all the symptoms of a general peritonitis, with hard, thready pulse and a temperature of 100°. Immediate operation was advised and the abdomen was opened by Dr. Hutchinson. A perforation the size of a penny was found in the ileum a short distance above the cæcum. Lymph was present over the intestine and fecal material in the peritoneal cavity. The appendix was inflamed and also perforated.

Numerous intestinal ulcers were visible through the walls of the gut. By May 29th the patient seemed perfectly con-

valescent. This was the first operative case to recover in the Pennsylvania Hospital. His perforation was evidently the result of a focal necrosis of the gut in the large ulcer so commonly seen near the ileocæcal valve. It is also interesting to note that in this case the appendix was perforated, and that the perforation occurred one month after an apparent convalescence and not during the relapse. This is, however, a difficult point to explain.

Case IX.—D. A., aged thirty-nine years; hospital No. 389; admitted May 4, 1902. *Typhoid fever, perforation, operation, two relapses,* and *recovery.* Discharged August 4th. Admitted to the surgical ward with the history of illness of ten days. There was no record of the physical signs present. Peritonitis was diagnosed, and on operation by Dr. Harte, eight ounces of lemon-colored fluid were found in the abdomen, the surfaces of the gut were congested, the appendix was removed, and on further search a perforation in the ileum was discovered. Widal was negative; leukocytes 7100. The temperature soon reached normal and remained down for seven days after operation. The man had a true relapse from twenty days after operation until the forty-seventh day—twenty-eight days of fever, and also a slight rise in temperature, 100° to 101° on the fifty-fifth to the seventy-third day. He left the hospital with an operative hernia which he absolutely refused to have repaired. This case was primarily looked upon by the surgeons as one of appendicitis, and was so operated upon. The appendix, however, although not absolutely pathological, was removed, and subsequent search revealed the intestinal perforation.

Case XI.—F. S., aged forty-three years; hospital No. 1567; admitted August 16, 1902. *Typhoid fever, perforative appendicitis, operation,* and *recovery.* Discharged October 10th. Admitted with history of illness of thirty-one days, with palpable spleen and soft, distended belly. On August 20th, the thirty-fifth day, he developed sudden abdominal pain and tenderness over the abdomen, with no special localization. The recti were rigid. Leukocytes rose to 9400, previous examination on August 16th showing them to have been 5400. Widal was negative. The pulse and respiration were not affected. Consultation resulted in diagnosis of perforative peritonitis. Operation showed free fluid, small perforation in ileum. On day of operation there was no dulness in the flanks, but liver dulness was present. The temperature chart has been lost. (Laboratory diagnosis: acute periappendicitis.)

Case XII.—E. S., aged thirty-five years; hospital No. 2079; admitted September 28, 1902. *Perforation, operation,* and *death* on October 9th. Admitted to a private room after illness of eight days. In bed three days before admission. The usual prodromes of typhoid; no mention of abdominal pain. Not very ill, but mentally depressed, and convinced that he would die. Had a temperature range of 102° to 103° for ten days. At 3 A.M. on the sixteenth day he had sudden pain in both testicles and in the abdomen. By 5.30 A.M. the pain was more intense and the abdominal pain general. Slight distention with slight abdominal tenderness without rigidity were present. The stools and discharges of flatus gave no relief. By 9 A.M. the right side was distinctly more rigid and dulness was present in the flanks. Leukocytes at this time were 6100. Consultation with Drs. Stengel and Gibbon, with diagnosis of perforation; operation at 11.30 A.M. Perforation in ileum; turbid greenish fluid in belly; peritonitis; death at 7 P.M. Partial autopsy.

Case XIII.—L. V., aged twenty-six years; hospital No. 2330; admitted October 20, 1902. *Perforation, no operation,* and *death* forty-five minutes after being taken into the receiving ward by ambulance. Sent to hospital with diagnosis of retention of urine and uræmia. Said to have been sick but forty-eight hours. Practically pulseless on admission, with tender, tense, and tympanitic abdomen. On catheterization no urine secured.

On autopsy but one typhoid ulcer was found in the ileum a short distance above the ileocæcal valve and a perforation the size of a ten-cent piece through its base; peritonitis.

Case XIV.—F. P., aged eighteen years; hospital No. 2408; admitted November 9, 1903. *Perforation, operation,* and *recovery.* Admitted with a history of a mild typhoid of thirteen days' duration. At 12 noon on the fifteenth day of his disease he had sudden severe abdominal pain, tenderness on the right side, spasm of the right rectus, costal respiration, and complete obliteration of the liver dulness. At 3.30 P.M. the leukocytes had risen to 17,500, at 5 P.M. they were 16,500, and at 7 P.M. 13,400. The temperature, which was 100° at the time of the first pain, fell to 99.2° at 1.30, P.M., remained the same at 2.30 P.M., and by 3.30 P.M. had risen to 102.3. By 7 P.M. it had reached 103.2°, with subsequent fall to 99.4°. The operation was performed eight hours after perforation, and showed free gas in the peritoneum, the presence of fluid, and a perforation in the ileum. This was a so-called typical case of perforation in which all the symptoms were present and the blood findings conclusive. This patient recovered.

Case XV.—R. P., aged twenty-eight years; colored; hospital No. 2454; admitted October 31, 1902. *Perforation, operation,* and *death* on November 6. Had chancre within two years, used alcohol freely, and had malaria several times. Admitted to medical ward after seven days illness characterized by headache, diarrhœa, and daily chills for five days. The urine showed hyalogranular casts, and the spleen was palpable. Had moderately severe attack. On October 3d, at 3 A.M., he was aroused from sleep by sudden abdominal pain (tenth day of disease) situated in both lower zones. This was the first abdominal pain complained of since his illness began. He vomited his milk; pulse became more rapid; the belly was not rigid, but generally tender. By 5.30 A.M. he vomited greenish mucus. There was moderate tympanites present, most marked in lower zones. Rigidity was now distinct, especially on the right side; slight tympanites. Doubtful movable dulness in the flanks. Breath sounds heard

distinctly over abdomen as low as umbilicus. Liver dulness was absent in midclavicular line, present in axillary line. Leukocytes at 6.15 A.M., 11,360. Operation by Dr. Mitchell at 7.30 A.M. Perforation in ileum six inches above ileocæcal valve the size of a slate-pencil. Death from general peritonitis. Autopsy.

CASE XVI.—F. P., aged thirty-nine years; hospital No. 2815; admitted October 5, 1902. *Appendicitis, operation, perforation,* and *death* on November 1, 1902. The previous history shows this patient had vague pains in the region of his appendix for eighteen months. He was admitted to a private room of the hospital on the tenth day of a typhoid, which began with a chill and was characterized at onset by unusual pain in the region of the appendix, mild fever, and for typhoid a high leukocytosis, 10,200 on the seventh day. For several days after admission the right iliac region was quiet, but on October 7th, the twelfth day, he had some tenderness over the appendix, with rigidity. The leukocytes at 4 P.M. were 14,900. A differential count at this time showed the polynuclear leukocytes ranging from 74 to 77 per cent.; the small lymphocytes, 17 per cent. The following morning the pain again recurred with severity; the leukocytes had risen to 18,400. Consultation, Drs. Lewis, Harte, and Le Conte, resulted in a diagnosis of appendicitis, with recommendation of operation. Appendectomy was done on the thirteenth day of his typhoid, and it was noted at this time that the ileum was much thickened and several typhoid ulcers were observed. He reacted well and was fed by bowel for thirty-six hours. Two days after operation (October 11th) he had a chill in the early morning, which was repeated at 8 P.M., both followed by profuse sweats. On the following day he exhibited some weakness after sponging, and the abdomen became distended. A differential count at this time showed the polynuclears 91.6 per cent.; the small lymphocytes, 4.2 per cent.; the large lymphocytes, 3.4 per cent. Blood culture the same day (seventeenth day of illness) showed a pure culture of typhoid bacillus. The wound showed no tendency to heal and gaped open. The stitches were therefore removed on October 14th. On the same afternoon there was considerable distention, which was not relieved by passage of rectal tube. The wound remained sweet, but still abdominal distention continued, and on October 18th (the twenty-third day of illness) both legs were noted to be tender and slightly swollen. He was tender over saphenous vein. Leukocytes had fallen at this time to 7300. Early on the morning of October 21st he complained of abdominal pain, with some distention, but without rigidity or tenderness. This distention was first here mentioned as being localized to the transverse colon, and continued on the following day; and on October 23d (the twenty-eighth day) he complained of severe pain in left side of the abdomen to the left of the umbilicus, which seemed to the patient(and he was an unusually acute observer) to be of peritoneal origin. It was, however, relieved after a bowel movement, only to return in the evening, with distention. On the next day, at 9 P.M., he again complained of severe pain; there was a tender area the size of a quarter of a dollar discovered to the left of the umbilicus. On the following day (the thirtieth) the abdominal distention was marked, mainly over the transverse and descending colon, in which peristalsis was visible, and an acute, cramp-like pain was felt when the peristalsis reached the tender area above. On this day the wound was again opened up and about eight to ten ounces of clear serous fluid escaped from the peritoneal cavity. The intestine seemed normal in appearance, and the examining finger inserted toward the site of pain detected no adhesions. He vomited at 2 P.M. and again at 6 P.M., and the temperature for the first time fell below normal, to about 97°, and the belly became greatly distended and very tender in the same left umbilical spot. This was probably the day of perforation. A general consultation of the attending surgeons and physicians of the hospital was held at this time, and the opinion was expressed that intestinal obstruction was present and that operative interference was necessary. After consultation, however, it was decided to have one of the surgeons present pass a rectal tube, which was done, and twelve ounces of olive oil introduced through it, followed by a soap-and-water enema. This resulted in the removal of a small amount of fecal material and some gas, and gave relief. On the following day the patient was decidedly improved, with a soft abdomen, while on October 27th (the thirty-second day) there was again distention, and on the day following this the abdomen was painless, flat, and the improvement general. On the evening of the twenty-ninth he again complained of some left-sided abdominal pain, and distinct distention of the transverse colon was present, while the epigastric region was concave. Two days later he had pain on pressure over the region to the left of the umbilicus, and again distention of colon with rigidity of either rectus. The finger of the surgeon was passed into the appendix wound, and immediately there was a puff of gas and some fecal material extruded from the wound. Perforation was diagnosed; operation was advised, and performed by Dr. Harte. There was found a large necrotic area, the size of a fifty-cent silver piece, on the posterior surface of the transverse colon, which was partially walled off by adhesions and exudate. The patient did not rally subsequent to operation, and died at 9 A.M. the following day.

This was a most difficult case—an early appendicitis in typhoid fever of moderate intensity. After operation the wound showed no tendency at all to unite, though it remained sweet. Then there developed chills, a mild phlebitis, and evidence of intensity of infection, which was feared might be surgical in character, but was not. The temperature behaved as one would anticipate in such a case. Abdominal pain of peritoneal type was felt on the twenty-eighth day of illness.

There was distention, and the temperature jumped from 100.2° to 103.2°, and the following day the leukocytes had

jumped from 8680 to 13,100, while on the thirtieth day there was a collapse which was in part considered due to the dressing of the wound. Perforation probably occurred on one of these days, and adhesions were being formed from this time on.

The symptoms were due to nature's attempt to wall off a large necrotic area of the transverse colon. In this case distention was mostly limited to the large bowel, a point worth bearing in mind.

Case XVII.—V. C., aged eighteen years; hospital No. 2940; admitted December 10, 1902. *Typhoid fever, perforation, no operation*, and *death* on December 23. In medical ward on eighth day of typhoid, onset characterized by fever and pain in abdomen. On admission the abdomen was somewhat distended, but soft and not tender; spleen palpable. Moderately severe case. On December 14th, the thirteenth day, passed a lumbricoid worm in stool. At 8 P.M. on December 16th, the fifteenth day, had severe abdominal pain, with marked tenderness and general resistance. At 7 P.M. he had a bowel movement, followed by another at 9.30 P.M., and was subsequently quiet and did not complain during the rest of the night. A study of the temperature chart is as follows: 7 P.M., temperature, 103.2°; pulse, 100; respiration, 28; 7.30 P.M., temperature, 103.2°; pulse, 96; respiration, 28; 10.30 P.M., temperature, 105.2°; pulse, 108; respiration, 16; 11 P.M., temperature, 104.3°; pulse, 104; respiration, 32.

At 9 A.M. the following day he had a second attack of pain, with general abdominal rigidity and tenderness. The breathing was costal. Tenderness most marked on the right side. Dr. Le Conte saw him at 11.30 A.M., when the leukocytes were 7400, liver dulness almost obliterated, and diagnosed perforation. Operation refused. Patient vomited once during the day and distention increased. Leukocytes on December 18th, 10,200; on the 20th, 8800; and on the 21st, 6600. He died on December 23d, at 12.25 A.M., with general peritonitis. Autopsy showed general fibrinopurulent peritonitis, perforation in ileum; no attempt at closure.

Case XVIII.—T. C., aged nineteen years; hospital No. 3321; admitted January 12, 1903. *Perforation, operation*, and *death* on January 29th. Five days ill before admission with severe infection. Temperature about 104°, and but little affected by tubbing. On the twelfth (?) day a slight hemorrhage occurred without affecting the general condition. On the nineteenth day he had sudden seizure of abdominal pain at 9.50 A.M., with decided rigidity of abdomen most marked on the right side. He had always been somewhat rigid. Chilly sensations were present. Breathing mainly costal. He had been constipated for three days, but had a large yellow movement that afternoon. He had pain during the afternoon and night, but slept from 8 P.M. to 4 A.M. Leukocytes at 4 P.M. were 4700, at 7 P.M., 5600. The following morning the belly was slightly retracted, and undoubted rigidity of right rectus and marked tenderness of the right upper abdominal zone was present. Leukocytes 7100. Operation at 4.30 P.M., by Dr. Le Conte. A small perforation was found twelve inches above the ileocæcal valve in the ileum. The man died in seventy-two hours from general peritonitis. Autopsy showed general peritonitis, and a perforation in ileum 20 c.m. from ileocæcal valve.

Case XIX.—M. R., aged twenty-three years; hospital No. 3258; admitted January 7, 1903. *Perforation, operation*, and *death* on January 19th. Admitted to the medical ward on the eighth day of typhoid, characterized by headache and malaise; bowels satisfactory. The abdomen was soft and painless. On January 15th (sixteenth day) she complained of some abdominal pain. There was no marked tenderness, and no rigidity or distention. She vomited on the following day, yet had no pain. At 6 A.M., on January 19th (the twentieth day) she suddenly collapsed, with small, imperceptible pulse and tympanitic abdomen, but no pain. Operation was performed, perforation in the ileum discovered. She died the same evening. There is no mention in this case, which was of a mild type, of the liver dulness, the leukocytes, the size and site of perforation by the operator. No temperature chart accompanies the history.

Case XX.—M. T., aged eighteen years; hospital No. 3548; admitted January 29, 1903. *Perforation, no operation, death* on February 7th. Sick for one week prior to admission, moderately severe case with acute bronchitis, rapid and dicrotic pulse. Had no abdominal pain until the fourteenth day of disease, when he complained of general pain and was unable to void urine. The pain increased, the pulse and respiration ran up, while no special change in temperature was immediately observed. At 1 P.M. the temperature was 103°, at 5 P.M. 104.2°, at 9 P.M. 100°, at 1 A.M. 99°, and at 5 A.M. 98.1°. A diagnosis of general peritonitis was evident. No operation was attempted. He died early on February 7th from general peritonitis. Fluid present in flanks; distention, with absence of liver dulness. Autopsy showed fibrinopurulent peritonitis, few feces in abdomen, and a small perforation 4 mm. 105 cm. above cæcum in the centre of a small transverse ulcer.

Case XXI.—W. J., aged thirty-seven years; colored; hospital No. 3557; admitted January 30, 1903. *Perforation, operation*, and *recovery*. Discharged March 18th. Ill two weeks of general malaise. One week before admission began to have severe abdominal pain, at first general, and later more severe in lower zones, especially on the right side. Vomited the evening before admission. Admitted to receiving ward with severe pain in abdomen, especially in lower right quadrant; somewhat distended, dull in flanks, generally tender, and more so in right iliac region; right rectus more rigid than left. Temperature, 101°; regular, full pulse. Appendicitis diagnosed; operation by Dr. Hutchinson. Free fluid in peritoneal cavity; pinhead perforation found twelve inches above cæcum. Surgical convalescence was good; temperature became normal by February 28th. There was no temperature chart appended to this history.

Case XXII.—J. O'C., aged fifty-two years; hospital No. 3665; admitted February 5, 1903. *Myocarditis, unsuspected perforation*, and *death* on February 10th. History of abuse of alcohol in recent years. Had been sick about one month before admission, and been attempting to nurse himself. Two weeks before admission had chills, with dyspnœa on exertion or excitement. The abdomen had been sore to touch for some time. He was somewhat delirious on admission, with weak, irregular, intermittent heart. No fever to speak of, temperature usually about 99°; the highest at any time was 100.2°; respirations, 26 to 28. Bowels were sluggish; no hemorrhages; had a flabby, enlarged, weak heart. On February 9th he was very delirious; uræmic (?). There was a sense of resistance in the right hypochondriae region. He winced on pressure over this area, and on the subsequent days there was some abdominal distention, with tenderness and slight rigidity. The pulse became rapid without change in the temperature, and death ensued. Neither typhoid nor perforation was suspected. Autopsy. There was found ulceration and perforation of the appendix, with healing ulcers of the ileum; general fibrinopurulent peritonitis; atrophic cirrhosis of the liver, with fatty degeneration of the heart and kidneys, and interstitial myocarditis. There was thrombosis of the omental veins, with hemorrhagic infarction of the omentum, especially the lower portion, which was really a firm, thick, hemorrhagic wad, measuring 1 c.c. to 2 c.c. in thickness. There were numerous small healing ulcers in the ileum.

Case XXIII.—J. K., aged twenty-six years; hospital No. 4160; admitted March 13, 1903. *Perforation*, *operation*, and *death* on March 20th. On admission he was considered to be in about the twentieth day of a typhoid of moderate severity. His attending physician considered he had had influenza for two weeks, which was followed by typhoid. The temperature range was about 103°; he had active bronchitis with blood-stained sputum. The belly was soft and not tender; he was not delirious. At 5 P.M. on March 15th (the twenty-fifth day) he had a slight chill, and by 5.30 P.M. seemed to have severe paroxysmal abdominal pain. He stated that he had had some pain since 2 P.M. He always was a very nervous patient about all symptoms since admission. During the pain he gritted his teeth. The respiration was thoracic; the recti were prominent and rigid, and the pain, which was general at 5.30 P.M., was most marked in the left zone. Liver dulness was absent in the midclavicular line. At 11 P.M. both flanks were noted to be tympanitic; he was quiet, but said he still had abdominal pain. Some rigidity was present, most marked on the left side. The abdominal muscles were used in respiration while he slept, but movement was restricted on full inspiration. Peristalsis was not heard. He had a fair night; was catheterized at 3 A.M., and after 9 A.M. the following day had considerable pain, especially about the umbilicus, with more muscular rigidity. The epigastrium was retracted. The leukocytes were 6250; the liver dulness was absent in the midclavicular line; present in the axillary line. Perforation diagnosed by Scott. Operation by Dr. Harte; cloudy fluid, with feculent odor present in the abdomen; upper part of small bowel collapsed, lower distended; pinhead perforation in ileum twelve to eighteen inches above cæcum; three to four hours after operation fecal vomiting set in, followed by distention and rigidity, and death early the following morning. The temperature, pulse, and respiration at time of perforation were as follows: At 5 P.M., temperature, 102°; pulse, 88; respiration, 24. Study of temperature: 5.30 P.M., temperature, 103°; pulse, 112; respirations, 24; 9 P.M., temperature, 102°; pulse, 88; respirations, 24; 1 A.M., temperature, 103.3°; pulse, 92; respirations, 28; 3 A.M., temperature, 99.1°; pulse, 100; respirations, 28.

Case XXIV.—C. S., aged twenty-eight years; colored; hospital No. 4163; admitted March 13, 1903. *Perforation*, *operation*, and *death* on March 25th. He entered on the fifteenth day of an enteric fever, having had four chills during the first week, and had been in bed but the day before admission. He was a well-developed negro, with rather severe infection. The temperature ranged between 104° and 102° for two weeks. There were blood clots in the stools on the twenty-first day, the belly soft on the following day, and no effect observed on general condition. On the morning of the twenty-fourth day slight tympanites was noticed, with tenderness on palpation, especially over the bladder. Dr. Harte saw him and advised against operation. There was no vomiting nor rigidity, and the facial expression was not bad. Later in the afternoon a small patch of bronchovesicular breathing was discovered at the right base, and the abdominal symptoms were then attributed to the pulmonary consolidation. He vomited during the afternoon, and by 6.30 A.M. on the following day the pulse and respiration were poor and rapid, and he had vomited large quantities of greenish liquid. The diagnosis of perforation was now decided upon, and operation performed by Dr. Harte at 11 A.M. The patient, however, died at 11.45. Autopsy. Seropurulent peritonitis; no pneumonia.

There was a small perforation 4 mm. in area in an almost gangrenous portion of the gut. There was a general peritonitis present. In this case the temperature shows no change on the twenty-third day, and on the twenty-fourth day rose to 101.1°, and the pulse and respiration rate kept going up.

Case XXV. C. J. N., musician, aged forty-nine years; admitted to private room 1903. *Typhoid fever, relapse, perforation, operation*, and *death*. Seen in consultation with Drs. Eshner and Gibbon. Seen May 15, 1903 after an illness of probably five or six weeks. After having had fever for several weeks he felt decidedly better, when his temperature again rose (relapse?), and on May 12th he bled rather freely from the bowel. On the following day abdominal pain of slow onset but gradually increasing in severity was complained of. The belly became slowly tympanitic. When seen at the Pennsylvania Hospital early on the morning of May 15th the spleen

was palpable, the recti were rigid, and tenderness was present, being greatest on the left side just below the umbilicus. The pulse was 112, the respirations shallow, and no abdominal respiration visible. The liver dulness was gone in the midclavicular line and present between the eighth and ninth ribs in the midaxillary line. Peristalsis was absent. The right flank was somewhat wooden on percussion. There had been no vomiting and no chill. Leukocytes, 22,000. Diagnosis of intestinal perforation was made, and Dr. Gibbon operated at 9.15 A.M. A perforation in the ileum the size of a black pinhead was found. Fluid and general peritonitis present. Operation consumed thirty minutes. The patient died sixty hours after operation, from general peritonitis.

Case XXVI.—D. P., aged twenty-two years; hospital No. 403; admitted May 4, 1903. *Peritonitis*, *operation*, *appendicitis*, and *death from pneumonia* on May 14th. He entered the hospital after an illness of nineteen days, characterized by headache, cough, fever, bloody sputum, diarrhœa, and pain in the right side of abdomen. On admission was considered seriously sick. The percussion note was impaired over the whole chest, without distinct areas of dulness. There were many large bronchitic and some fine mucous rales heard over the chest. The abdomen was distended; there was pain and some tenderness in the right iliac region; no rigidity of recti. Leukocyte count was low, 5600. On the second day after admission, twenty-first day of the disease, the abdomen was more distended and rigidity more marked on the right side, and he complained of general abdominal tenderness, which was most marked in the lower zones. The flanks were clear and liver dulness present. Pulse increased in rate and the leukocytes rose to 7200. On consultation a diagnosis of probable perforation was made, and Dr. Gibbon operated. No perforation was found, but the appendix was inflamed, tense, and much thickened, and it was considered wise to remove it. The patient did fairly well for twenty-four hours after operation, but on the second day the lungs were filled with rales, scattered areas of tubular breathing were heard, and the right base consolidated. He died on May 14th, the twenty-eighth day of his disease, presumably from the pulmonary complications.

Case XXVII.—J. G., aged thirty-two years; hospital No. 445. *Hemorrhages*, *perforation*, *operation*, and *death* on May 18, 1903. This patient was an orderly in the medical wards of the hospital, and when admitted to the ward was supposed to be in the eighth day of his illness. He had nausea, vomiting and pain in the back and abdomen, with marked nervous symptoms. The abdomen was slightly distended and tympanitic without rigidity. He complained of slight tenderness in the right iliac fossa and below the left costal border. Two days after admission the abdomen was distended, while the pain and tenderness were somewhat improved. On May 11th, the fourteenth day of the disease, he had profuse diarrhœa, and blood clots were present in the stools, with some abdominal distention. The following day, and in fact until May 17th, the twentieth day of his disease, he continued to pour blood from the bowel. The pulse was weak and almost imperceptible at the wrist, and operation, after consultation with Drs. Lewis and Harte, was decided upon to control the bleeding. On opening the abdomen a perforation was found in the ileum ten inches above the ileocæcal valve. The intestinal canal was filled with blood clots. The man died twenty-two hours after operation.

This is, I think, one of the first cases to be operated upon for the relief of hemorrhage in typhoid fever, a suggestion which has been made with some degree of force recently before the American Medical Association by Dr. James C. Wilson. In this case the perforation found was not suspected.

Case XXVIII.—E. N., aged twenty-nine years; hospital No. 605; admitted May 20, 1903. *Perforation*, *operation*, and *death* on June 1st. Entered the medical ward on the seventh day of typhoid, with rather a scaphoid belly. The temperature ran about 103°, and was well controlled by baths. On the morning of May 31st (the seventeenth day) he complained of pain in the abdomen, without rigidity or distention being noted. At 2 A.M. the following day he vomited copiously a thick, greenish liquid; had severe pain in the abdomen, with a moderate amount of rigidity, and no distention. The pulse and respiration rate were increased. At 5.30 A.M. he was much worse in every respect. Diagnosis of perforation made; operation by Dr. Harte at 6.30 A.M. Purulent fluid was found in the abdomen; lymph on the intestines and a perforation in the ileum. Size and location not stated. The man was in very poor condition after operation, and died at 1 P.M. the same day. In this case nothing is to be learned from a study of the pulse, respiration, and temperature range. Autopsy showed a perforation 23 cm. above the cæcum; fibrinopurulent peritonitis; swelling of mesenteric glands; splenic tumor; apical tuberculosis, small cavities, both apices.

Case XXIX.—T. W., aged twenty-four years; colored; hospital No. 627; admitted to hospital May 26, 1903. *Typhoid fever, large hemorrhages, perforation, operation*, and *death*. He entered the hospital on the ninth day of illness, characterized by all the premonitory symptoms of typhoid fever. On May 27th, or the tenth day of his disease, he had several enormous hemorrhages without however seriously prostrating him. On the thirteenth day, however, he again bled freely, after which his illness assumed a more benign course, though he complained at this time of slight abdominal pain below the umbilicus, without, however, either rigidity or tenderness. The pulse was rapid and feeble. On June 9th, or the twenty-third day of his disease, he had sharp, cramp-like pains in the abdomen without abdominal rigidity, followed by vomiting. The temperature rose from 102.1° at 5 P.M. to 105° at 1 A.M. By 9 A.M. the next day it was 98.4°, at which time the pain was more severe, and the abdomen rigid with marked tenderness along the right rectus. He perspired freely and was extremely nervous. Perforation was diagnosed and operation performed by Dr. Harte eighteen hours after, showing purulent

fluid in the pelvis and along the ascending colon. A rather small perforation was found in the cæcum. The patient died of general peritonitis in thirty hours. No autopsy.

Case XXX.—M. de M., aged twenty-six years; hospital No. 677; admitted to medical ward on May 26, 1903. *Perforation, operation*, and *death* on June 10th. He had a typhoid of moderate severity, with history of eight days' illness. Sordes on teeth and lips. Soft and somewhat tympanitic abdomen, without muscular rigidity. He complained of some pain and tenderness in the right iliac region. He was mildly but constantly delirious after admission. The pain in the right iliac region was still complained of during the first week. On June 3d, the fifteenth day of his illness, he had a severe chill in the morning without discoverable cause. This was followed by a rise in temperature to 107.1°. There was also a second chill at 9 P.M. On the following two days he had severe chills without discoverable cause. No malarial organisms were found in the blood; the leukocytes were 7700; no phlebitis or cholecystitis present. On June 6th, the eighteenth day of the disease, he complained of acute pain and tenderness in the right iliac region, which was greatest over the appendix region. The right rectus muscle was rigid, more so than the left, and there was some distention present. Upon this and the two following days he had chills. By the evening of the nineteenth day of illness the abdomen was extremely tender, decidedly rigid, while the pain was intense. By the following morning, the twentieth day of the disease, the abdomen was board-like, with marked tenderness over both lower zones. He was seen in consultation by Dr. Harte, and his condition was regarded so serious as to preclude operation. Owing to a change, however, for the better in his pulse, operation was decided upon, and was performed at 5 P.M. the same day. Thin, purulent fluid was found in the peritoneal cavity, while a perforation was discovered about twelve inches above the ileocæcal valve. Death occurred from general peritonitis thirty-six hours later. Autopsy: Ulceration in transverse colon; deep and extensive ulceration in ileum; 60 cm. from cæcum is point of perforation. There was complete thrombosis of the vena cava from a point 9 cm. above union of the iliac veins, which extended partly in external iliac and femoral veins.

In this case the temperature behaved in a most erratic way for several days before perforation occurred. This was, of course, due to his chills, which in all probability were due to the intensity of his infection and not to any complications. The acute pain which he had was experienced about or shortly after his chills, which were characterized by an acute rise in his temperature, followed by a return to its usual range. Nothing can be learned from the study of his chart so far as the temperature goes.

Case XXXI.—J. S., aged eighteen years; hospital No. 696; admitted to hospital May 28, 1903. *Perforation, operation* and *death* on May 31st. Admitted to the ward with history of an illness of four weeks; in bed two weeks. Had headache, fever, nausea, vomiting, and diarrhœa, but no blood. Considerable abdominal pain. Had been delirious for one week. He was a poorly nourished, anæmic-looking boy. The abdomen was somewhat distended, without rigidity, rose-colored spots present, making the duration of his illness seem doubtful. Complained of pain and tenderness in the right iliac region. On the following morning the abdomen was rigid, without distention, while he had decided pain and tenderness in the right iliac region. The temperature fell from 103.4° at 1 A.M. to 99.4° at 9 A.M. The pulse and respiration ratio had gone up. Consultation resulted in the diagnosis of perforation, and operation was decided upon and performed at 1 P.M. Perforation was found in the ileum the size of a pinhead. There is no mention made in the notes of the liver dulness. During the following twenty-four hours he was restless, delirious, and died about twenty-seven hours after operation.

Case XXXII.—C. E., aged twenty-five years; hospital No. 744; admitted June 4, 1903. *Supposed tuberculosis, undiagnosed perforation*, and *death* on June 22d. The previous history showed he had a cough extending over many years, with mucopurulent expectoration. For ten days prior to admission had fever, with prostration and cough. Bubbling rales were present over both lungs. No consolidation was considered present, and the heart was satisfactory. The leukocytes on the day after admission were 11,900. The fever was never high, and the chart shows no unusual rises or falls. Consolidation of the lung was first noted on June 20th, and signs of a cavity on the following day. He was supposed to have had a tuberculosis, though no tubercle bacilli were demonstrated in the sputum, and the lung condition was either not noted carefully or was overlooked. He died on June 22d, apparently from exhaustion. About a week before this time he had three liquid stools in the twenty-four hours, and this continued for some four days. Nothing unusual was noted about the abdomen, and four days before his death his temperature had reached the normal.

At autopsy the following conditions were found: typhoid fever, ulcers of ileum, adhesions between base of several ulcers and visceral peritoneum, pneumonia and gangrene of right lung; acute splenic tumor. There was bronchiectasis and cavities in all the lobes of right lung. There was no fluid in the peritoneum. There was an ulcer in the ileum 40 cm. above the cæcum, at the base of which there were dense peritoneal adhesions to another portion of the ileum and also a few centimetres lower down, firm adhesions attaching the bowel to the bladder. There were altogether three perforations thus closed. The ulceration was severe and deep, and a second ulcer was 25 cm. above the cæcum and a third one 18 cm. All had been firmly closed, with no evidence of peritonitis.

This case is one of great interest and extremely difficult of diagnosis. A man with a chronic pulmonary disease, bronchiectasis and gangrene of the lung, upon whom was grafted

a typhoid fever, who perforates without special evidence of abdominal pain, and died not from his typhoid or perforation but from the chronic disease. Perforation was never suspected in this case nor was typhoid.

Case XXXIII.—M. J., aged thirty-three years; hospital No. 762; admitted June 6, 1903. *Perforation*, *operation*, and *death* on the day of admission. Brought to the receiving ward with a history of having been sick with pain in the abdomen since June 1st. The pain began while he was at work; bowels had not moved for four days; vomiting had been present, but ceased the day of admission. The man was in a cold sweat, with weak, wiry pulse and cold extremities. There were large, moist rales at the base of the left lung. The respiration was costal; both liver dulness and splenic dulness were absent; the recti were rigid, and he complained of much pain in the right iliac region and just below the umbilicus. Tenderness was extreme in the right lower zone. Operation by Dr. Stewart. Milk-curds and feces were discovered in the abdomen, and a perforation large enough to admit the tip of the little finger was found eighteen inches above the cæcum. He died fifteen minutes after the operation was finished. No results from the temperature or pulse records in this case. Patient had no previous illness before perforation occurred.

Case XXXIV.—J. P., aged forty-two years; hospital No. 771; admitted June 7, 1903. *Perforation*, *operation*, and *recovery*. Discharged July 6th. Brought to the receiving ward with an indefinite history of acute constipation beginning four days before; continuous vomiting for twenty-four hours. The belly was rigid and tender; he had a reducible hernia on the left side. Two inches of liver dulness were present in the midclavicular line. Splenic dulness was somewhat increased. He was probably walking about forty-eight hours before admission. There was no definite surgical diagnosis made. Peritonitis was evident. Operation by Dr. Stewart showed the peritoneal cavity filled with cloudy fluid containing flakes of lymph without any decided odor. Intestinal perforation discovered "thirty-six inches or more above cæcum" (history note). The temperature reached normal six days after operation (in fact it never was above 101.3°) and remained down. The circulation was always satisfactory. This is an interesting case, illustrative of perforation of the intestine without a previous or subsequent febrile attack. Three days after operation the Widal was suggestive and the leukocytes 12,100. The leukocyte count subsequently dropped to 9100 and the Widal became positive. The man made a satisfactory recovery.

Case XXXV.—J. H., aged thirteen years; hospital No. 890; admitted to hospital June 19, 1903. *Perforation, operation*, and *recovery*. When admitted had an illness of thirteen days. Typhoid of moderate severity; some nocturnal delirium with slightly distended abdomen without rigidity. On June twenty-first, the fifteenth day of illness, complained of severe pain in left iliac region in the early morning, lasting but a few moments. Later, there was tenderness over the whole lower abdomen, with slight rigidity, without distention. There was a slight increase in the pulse rate, without corresponding respiratory disturbance. The following day he had a chill; still complained of abdominal pain, which was now more severe on the right side, with marked rigidity. Following the chill he had a second severe attack of pain, which was characterized by a rise in temperature to 105.3°, with subsequent fall to 101°. Consultation, with diagnosis of perforation. Operation performed, which showed cloudy fluid in peritoneal cavity and a small perforation in the ileum. Condition good at the end of operation. This patient recovered after a rather uneventful surgical convalescence.

Case XXXVI.—J. E., aged thirty-seven years; hospital No. 1208; admitted July 20, 1903. *Perforation undiagnosed, but discovered at autopsy*, and *death* on July 31st. Entered the medical ward on the seventh day of typhoid; temperature range of 103°; abdomen on admission was slightly rigid, without marked tenderness. He seemed to have a mild attack and appeared to be convalescent. By July 28th (the fifteenth day) his temperature fell to 100° and remained there or lower. The pulse was good. That day blood was noted in the stools, which were watery. He refused to reply to any questions. During the evening of July 30th the hospital notes state that he "grew worse," and died early the following morning. A study of the temperature chart in this case shows no special change in either the temperature, pulse, or respiratory rate. At 7 A.M on the thirtieth day the temperature was 99.1°; respirations, 24; pulse, 112. At 10 A.M. the temperature was 103.2°; respirations, 28; pulse, 144. The temperature, however, again fell during the afternoon, as well as the pulse and respirations, and subsequently jumped up again and remained until death. At autopsy a perforation in the ileum, ½ cm. in diameter, 125 cm. above the cæcum, was discovered, which was entirely unsuspected during the life of the patient; general peritonitis, fibrinopurulent and hemorrhagic.

Case X.—B. C., aged twenty-two years; hospital No. 1438; admitted August 10, 1903. *Typhoid fever, perforation, no operation*, and *death* on August 22d. Entered the medical ward on ninth day of illness, characterized by high temperature with soft, frequent pulse, running about 112. The abdomen was soft; the spleen very large; many rose spots. Had a hemorrhage on the sixteenth day, without any fall in temperature, but increase in the rate of pulse. On the eighteenth day, between 10 P.M. and 7 A.M., the temperature fell from 103° to 98.2°. There was a second tarry hemorrhage on the following morning. At the same time the abdomen became distended and rigid. Liver dulness was absent; there was no local tenderness. Leukocytes were 6800. On the following day the abdominal condition was about the same, though the distention was greater and the rigidity less. Just before his death, which occurred on the twentieth day, a third hemorrhage occurred. The temperature remained below 99° after 7 A.M. on the nineteenth day until 2 P.M on the twentieth day.

A diagnosis of perforation was not made. The pulse was always rapid.

Autopsy showed the presence of a purulent peritonitis, with gas and feces in the abdomen. The intestines were more or less collapsed, so that a great space existed between them and the abdominal walls. On opening the intestines the ileum was found to be the seat of extensive and deep ulceration. There were four perforations: the first, 5 cm. above the ileocæcal valve, was of minute pinhead size; two very large ragged perforations were present in the large ulcer, immediately above the one already mentioned, which measured about 1 cm. by 2 cm. in length, and they have their long axis running about the intestine; the fourth perforation was found 35 cm. above the ileocæcal valve, while the last ulcer was situated 46 cm. above the cæcum.

Case XXXVII.—P. de S., aged twenty-five years; hospital No. 1460; admitted August 11, 1903. *Perforation*, *operation*, and *death* on August 24th. Entered medical ward on twentieth day of typhoid, characterized at onset by daily chill at 1 P.M., with some abdominal pain; constipated; the spleen was palpable and tender; no malarial parasites were found in the blood; temperature range was about 102° or lower, and was easily reduced by sponges. At 7.30 A.M. on August 22d (thirtieth day) he complained of exquisite pain in the abdomen; the recti were rigid; pulse 120; temperature dropped; leukocytes were 11,500. Perforation diagnosed. Operation done by Dr. Gibbon at noon. Small amount of cloudy fluid and one or two milk clots were found in abdomen. A perforation large enough to admit a slate-pencil was found two inches above the cæcum. At the ileocæcal junction a large area of ulceration was noted, which at one point was very near rupture. He died of peritonitis, at 4.45 P.M. on August 24th, fifty-two hours after operation. Partial autopsy showed the primary perforation tightly closed, but a second perforation had occurred at the ileocæcal junction previously noted.

Study of temperature: 6.30 A.M., temperature, 102.4°; pulse, 106; respirations, 28. At 7 A.M., temperature, 99°; pulse, 96; respirations, 24; at 10 A.M., temperature, 102.2°; pulse, 120; respirations, 28. The patient had no chills after admission until within two hours before his death.

Case XXXVIII.—A. G., aged twenty-one years; hospital No. 1602; admitted August 25, 1903. *Perforation*, *operation*, and *recovery*. Discharged November 2d. Entered the medical ward on the tenth day of typhoid. The temperature was high at the start, but was soon controlled by baths. The abdomen was soft and not tender; spleen readily palpable and tender; active bronchitis. At 6.30 P.M. on August 31st (sixteenth day) he complained of sharp pain on the right side of the abdomen, which was very tender; the recti were somewhat rigid; he had neither chill nor vomiting. By 9 P.M. all the symptoms had increased in severity; leukocytes were 9600. Perforation diagnosed; operation by Dr. Mitchell. Perforation in the ileum discovered.

Study of chart: 5 P.M., temperature, 101.3°; pulse, 92; respirations, 24. At 5.30 P.M., temperature, 100°; pulse, 110; respirations, 24; at 9 P.M., temperature, 104.1°; pulse, 114; respirations, 24. This patient made a good surgical convalescence; the temperature fell and remained down seven days after operation, or the twenty-second day of illness. A true relapse occurred on the thirty-third day, with gradual febrile ascent, and fall by the fifty-first day. He made a good convalescence, however, marked by swollen feet, with tender toes and calves.

Case XXXIX.—B. M., aged eleven years; colored; hospital No. 1622; admitted August 26, 1903. *Hemorrhages*, *perforation*, *operation*, and *death* on September 22d. Entered the medical ward on the twenty-sixth day of a typhoid which had been characterized by repeated chills and sweats, with constipation, frequent vomiting, and some abdominal pain. She had been in bed two weeks before admission, and it is probable from the temperature chart that the duration of her illness was due to an intercurrent relapse. On September 13th (forty-fourth day) she passed some blood in the stool. Up to this time she had had fifty-seven baths. After the hemorrhage there was slight abdominal pain without distention. On the following day (forty-fifth day) her condition was unaltered, but some time between 10 A.M. and 11 A.M. she cried out with sudden pain, and put her hand to the abdomen. There was severe pain, with great tenderness and slight rigidity. Respiration was painful. There was no change in pulse, respiratory rate, or in the temperature. The leukocytes at 12.30 P.M. were 6700. The pain and tenderness steadily increased; perforation was diagnosed, and at 4.45 P.M. Dr. Gibbon operated. The abdomen remained rigid under anæsthesia. A perforation the size of a slate-pencil three feet (115 cm.) above the cæcum was found. A large number of intestinal ulcers and enormous mesenteric glands were noted. She did well the day following the operation; no evidence of peritonitis. On the second and fifth days after operation, however, she had hemorrhages, which did not seem to affect her very seriously, but the discharge from the wound was noted to be turbid and foul-smelling. She complained considerably of abdominal pain; the pulse failed, and she died at 2 A. M. on September 22d.

The autopsy showed that the original perforation was tight, but that a second perforation, 4 mm. to 5 mm. in diameter, had occurred. There is nothing to be learned from the study of the temperature chart in this case.

Case XL.—M. D., aged nineteen years; hospital No. 1676; admitted August 31, 1903. *Hemorrhages*, *perforation*, *no operation*, and *death* on September 6th. Admitted on the fourteenth day of typhoid. She had had hemorrhage of the bowels a few days prior, and had also had abdominal pain and vomiting. On the morning of September 3d (sixteenth day), following several days in which she had passed enormous quantities of blood in the stools, it was noted there was slight rigidity in the right iliac region, with some tenderness on pressure. The day before this the leukocytes were 6400.

On this day they were 7550, and on the fourth day, 5700. On September fifth (the eighteenth day) she still complained of much tenderness in both iliac fossæ. Dr. Gibbon had consulted with Dr. Charles Hart in this case, and considered it advisable not to operate. The woman was unable to retain nourishment either by month or rectum. On this same night, and during the early morning hours of September 6th, she had three hemorrhages. There was no abdominal tenderness, distention, or pain. The pulse was almost imperceptible; hypodermoclysis and stimulation were of no avail. She died at 6.20 A.M. on September 6th. Autopsy showed large areas of ulcers in both the ileum and colon, and one perforation in the ileum. In this case the pulse had always been extremely rapid from admission, 136 to 146, and the temperature behaved as one would anticipate a hemorrhagic case would do. The respirations were never high.

Case XLI.—J. S., aged thirty-eight years; hospital No. 1771; admitted September 8, 1903. *Typhoid relapse, perforation, operation*, and *recovery*. Discharged October 23d. This man was in the Pennsylvania Hospital in his primary attack, which was mild, from July 21st to August 17th, twenty eight days in all. It ran a temperature for only twelve days. After his discharge he was at home about one month, and was again admitted with all symptoms of a relapse, fever, palpable and tender spleen, with round, soft abdomen, which was, however, somewhat tender. On the evening of September 15th, the eleventh day of relapse, he reported to the nurse that he had been suffering all day with pain in the abdomen. At 10.30 P.M. he was sweating profusely, with anxious expression, rapid pulse, and chilly sensations. The belly was tympanitic, the recti rigid, and he was very tender, especially on the right side. Perforation was diagnosed, but operation delayed until 2 A.M., on account of securing permission from his friends. Operation performed by Dr. Le Conte. There was free fluid in the belly; perforation in the ileum, large enough to admit a probe, eight inches above the cæcum, in the midst of a necrotic area of considerable size. In two days he was in good condition, although he vomited considerably after the operation. Cultures from fluid showed streptococci pyogenes and also a few staphylococci pyogenes aureus. Wound healed promptly, and he was discharged on October 17th.

Study of temperature: 5 P.M., temperature, 101.1°; pulse, 128; respirations, 34; 9 P.M., temperature, 97.3°; pulse, 100°; respirations, 24; 12 midnight, temperature, 97.4°; pulse, 140; respirations, 40.

Case XLII.— H. C., aged twenty-eight years; hospital No. 2150; admitted October 12, 1904. *Typhoid perforation, operation*, and *recovery*. Discharged January 4th. Entered medical ward on eighth day of typhoid, the onset of which was marked by fainting attacks and daily chills until the day of admission. Had some abdominal pain. The belly was normal, the spleen palpable; he had a chill the day of admission, followed by high temperature. No malarial parasites were discovered after a careful search. The temperature range was high, though he responded readily to tubbing, but had frequent chills after being in the water. The baths were stopped on October 16th and sponges substituted, from which time he had no chills. On October 15th, the eleventh day, he complained a great deal of abdominal pain. Nothing, however, developed. On October 25th, the twenty-first day, he had a small hemorrhage without affecting his general condition. He was delirious at times and very stupid. On October 30th, the twenty-sixth day, at 5.30 P.M., he cried out with pain in the right side below the level of the umbilicus, but radiating through the abdomen. No rigidity was present, and a hot-water bag gave relief. (The abdomen was normal in the morning.) Two hours later there was slight rigidity of both recti, especially the right. He vomited greenish fluid. The pain continued at intervals, and his condition remained the same until between 2 A.M. and 3 A.M. The leukocytes were 5900. At 3 A.M. he had another paroxysm of pain and tenderness, and the abdomen was slightly distended, the liver dulness gone, and the flanks were clear. There was but little or no impairment of abdominal breathing and distinct rigidity of the right rectus. Dr. Mitchell made a diagnosis of typhoid perforation or appendicitis. Operation at 3.30 A.M. by Dr. Mitchell. Cloudy fluid in abdominal cavity, perforation the size of the head of a lead-pencil eighteen inches above the cæcum in the centre of an ulcer the size of a five-cent piece. The man reacted well and gave the attending surgeons no concern at all. On the eighteenth day after operation, November 18th, a fecal fistula developed, accompanied by slight fever. He was about the ward by December 9th. Study of the temperature chart: 5 P.M., temperature, 100.2°; pulse, 92; respirations, 24; 9 P.M., temperature, 99.3°; pulse, 136; respirations, 34; 10 P.M., temperature, 99.4°; pulse, 128; respirations, 36; 11.30 P.M., temperature, 99°; pulse, 118; respirations, 36; 10.30 A.M., temperature, 98.4°; pulse, 118; respirations, 32; 1.30 A.M., temperature, 100°; pulse, 120; respirations, 30; 2.30 P.M., temperature, 99.4°; pulse, 120; respirations, 30.

Case XLIII.—M. D., hospital No. 2175; admitted November 6, 1903. *Symptoms of peritonitis, perforation, operation, ruptured mesenteric gland*, and *recovery*. When admitted he was in the thirty-first day of a typhoid fever. He was a large, muscular Polander. On the thirty-third day he complained during the night of abdominal pain. The temperature, which had at 1 P.M. been 104.3°, fell during the afternoon and evening to 98° at midnight. The pulse was not changed, the belly was flat, and respiration easy. There was localized tenderness in the right iliac region, with some marked rigidity of the right rectus. There was no continuous pain. Early the following morning there was again very severe pain, with increased tenderness and rigidity in the right iliac region. The temperature remained low, below 99°, the leukocyte count remaining at 3500. The pulse was not affected. The liver dulness was present. Diagnosis of peritonitis, probably perforative, was made, and operation performed at 10.30 A.M.,

about five and a half hours after the second attack of pain. A peritonitis was found, involving the root of the mesentery, and a ruptured mesenteric gland was discovered near the ileocolic attachment of the mesentery, the gland substance free in the peritoneal cavity, cultures of which proved sterile. There was no perforation of the bowel. A large ulcer at the ileocæcal junction, covered with lymph, thick and yellowish, was turned in. The man made a good convalescence.

This case has been reported by Dr. R. G. Le Conte in detail in the *Journal of the American Medical Association*, October 24, 1904.

Case XLIV.—J. J., aged twenty-eight years; colored; hospital No. 2215; admitted October 18, 1903. *Perforation, operation,* and *death* on November 1st. He is said to have had typhoid fever five years before. Admitted on the ninth day of typhoid, characterized by general body pains, headache, marked constipation, and some fever. The temperature ran rather high. He was unable to retain milk, but took albumen-water and broths well. On October 29th (the twentieth day) he vomited at 9 A.M., and complained of slight abdominal pain. At 9.45 A.M. the belly was relaxed, pain less, without rigidity or distention, and temperature low. The general condition was excellent. At 10.15 A.M. the same night he felt a sharp, sudden pain in the right side of the abdomen especially at umbilical level, which later became general. At 10.30 A.M. he was sweating; pulse, 120; respirations, 36; temperature, 98°. He had an involuntary stool, and vomited greenish material. The belly was distended; both recti rigid; liver dulness was absent; dulness in the right flank. The abdomen moved with respiration. The leukocytes were 5900. On admission they had been 12,800. Perforation diagnosed. Operation by Dr. Hutchinson at 12.15 P.M. A perforation of slit-like character was discovered six or eight inches above the cæcum. There was an attempt at closure by overlying lymph, but two small perforations, the size of pin-heads, permitted fecal material to ooze into the peritoneal cavity, which contained a considerable amount of cloudy fluid. After operation the patient was extremely delirious, with constant subsultus. He died the next day at 4 P.M., without evidence of peritonitis.

The temperature and pulse study at the time of perforation was as follows: 9 A.M., temperature, 100.4°; respirations, 26; pulse, 100; 10.20, temperature, 98.3°; respirations, 32; pulse, 120; 11.20 A.M., temperature, 97.4°; respirations, 30; pulse, 112. The morning temperature showed nothing.

Case XLV.—W. W., aged fifty years; hospital No. 3646; admitted February 26, 1904. *Typhoid, subsequent perforation, no operation,* and *death* on March 6th. Entered medical ward on the sixth day of a doubtful typhoid, which began with a chill and cough, with frothy expectoration. On admission he had the signs of an active bronchitis; the belly was soft. He was very delirious. On the twelfth day the abdomen was much distended, without any marked change in the general condition. He became, however, decidedly worse, and on the following day he had a sudden severe attack of pain in the right side of the abdomen. The right rectus was rigid; after bowel movement the pain lessened. The liver dulness was normal. Abdominal breathing was not abolished. On the fourteenth day there was general abdominal tenderness, with some impaired resonance over the base of the right lung. On this day the leukocytes at 3 A.M. were 7200; the following day at 12.30 P.M. they were 2900. There was general abdominal pain, with great distension and increasing weakness. Death occurred early on the morning of the fifteenth day. There was no operation. There were no hemorrhages and nothing in the temperature worthy of special note. The respiration became more rapid after the twelfth day, jumping from twenty-eight to thirty-six, and so continuing.

Autopsy showed perforation in the large ulcer just above the cæcal valve; general peritonitis; free pus along ascending colon and extending up to liver.

Case XLVI.—E. G., aged forty-nine years; hospital No. 3720; admitted March 3, 1904. *Perforation, operation,* and *death* on March 23d. Entered the hospital with mild attack of typhoid. On the eighteenth day of disease she had intermittent pain, localized in the right iliac region, which became more severe on the following day, with tenderness on palpation, and especialy below and to the right of the umbilical level there was rigidity of the recti. There was no dulness in the flanks. The belly became tympanitic, and the following day the tenderness was more marked on the right side, but generally present. No chills, sweats, or hemorrhage present. Liver dulness was absent in midclavicular line, but was present from the eighth to tenth interspaces in the axilla. The leukocytes on admission were 4600, and on day of perforation 4800. Dr. Scott diagnosed perforation, and Dr. Gibbon operated within an hour. General peritonitis was present. There were five small perforations in the ileum, within eighteen inches of the ileocæcal valve, and one in the cæcum. The woman lived for nine days after operation, and died from cardiac failure.

This case probably perforated at least twenty-four hours before operation. On investigation it was learned that she had complained of pain on the previous day, which had not been reported to the resident or to the visiting physician. There was nothing in the temperature or pulse which was significant. The pain she had was more or less general and not very severe. She showed surprising resistance after operation, and continued to live for days, although the pulse could scarcely be felt at the wrist. There was no systemic evidence of general peritonitis.

Case XLVII.—R. B., aged twenty-four years; hospital No. 3890; admitted March 18, 1904. *Typhoid fever, perforative appendicitis, operation,* and *death* on April 17th. Entered the medical ward on the eighth day of a mild typhoid, characterized by chills and fever, with some abdominal pain and tenderness. Patient had a mild case. The abdomen was

noted as somewhat tympanitic though soft and somewhat tender. By the seventeenth day he seemed convalescent, but relapsed on the nineteenth day with gradual ascent of temperature. On April 11th (thirty-second day) he complained of pain in the abdomen, apparently greater on the left side, while the recti were slightly rigid. No distention was present. On the next day the trouble had disappeared. On April 16th (thirty-sixth day), at 6.45 P.M., he had severe pain in the right iliac region, and complained of being cold, but had no distinct chill or sweat. There was localized pain over the appendix and both lower zones. There was some spasm of the recti. The leukocytes were 5000. After 6.30 P.M. he had two subsequent attacks of pain. Consultation with chief resident physician and Dr. Hutchinson; diagnosed perforation. Operation at 12.30 A.M. Peritonitis was found. The appendix was perforated; no perforation of ileum; death thirty hours later; peritonitis. Autopsy.

The study of the temperature, taken hourly, was as follows: 5 P.M., temperature, 100.3°; pulse, 100; respirations, 24; 6.45 P.M., temperature, 102°; pulse, 116; respirations, 24; 7.45 P.M., temperature, 103°; pulse, 108; respirations, 24; 8.45 P.M., temperature, 103°; pulse, 114; respirations, 24; 9.45 P.M., temperature, 103.4°; pulse, 132; respirations, 32; 10.45 P.M., temperature, 103.4°; pulse, 116; respirations, 28; 11.45 P.M., temperature, 102°; pulse, 120; respirations, 32.

CASE XLVIII.—J. C., aged twenty-four years; colored; hospital No. 377; admitted May 2, 1904. *Hemorrhages, perforation, operation,* and *death* on May 19th. Previous history of alcoholism (?) and indefinite venereal infection. Admitted to medical ward with illness of eight days, characterized by abdominal pain, headache, and cough, with yellow sputum. Belly was soft and not tender, yet the day after admission the patient complained of abdominal pain, though examination developed no tenderness or rigidity. At 8 P.M. of the fifteenth day he had a hemorrhage of twenty-six ounces, which was repeated on the following two days in smaller quantities. On May 14th the blood showed a leukocyte count of 19,800 and a haemoglobin of 68 per cent. He had had three hemorrhages on May 13th and 14th, losing a total of seventy ounces of blood. At 9.50 A.M., May 23d, the abdomen was found to be slightly rigid, without tenderness. Half an hour later he cried out with sharp pain in the right iliac region. He was now very sensitive on palpation in the right lower zone. There was no change in the pulse rate, which since his repeated hemorrhages had been weak, small, and rapid. The liver dulness was present. The flanks were resonant. The leukocyte count at 11 A.M. and 12 M. was 6300 and 5900 respectively. Consultation with Drs. Lewis, Scott, and Harte resulted in a diagnosis of perforation. Operation at 1 P.M., when the presence of a pinpoint perforation eight or ten inches above the cæcum was found, with a small amount of free feces in the abdominal cavity, and peritonitis. Died in sixty hours, with probable asthenia. No symptoms of peritonitis. Respirations became very rapid.

CASE XLIX.—I. B., aged fourteen years; hospital No. 504; admitted May 13, 1904. *Typhoid fever, perforation, operation,* and *death* on May 29th. This patient was probably in the third week of typhoid fever when admitted to the surgical wards. Three days before admission he had sharp, sudden pain in the abdomen. He was brought to the receiving ward of the hospital on May 13th, with the primary diagnosis of appendicitis. After being seen by Dr. Harte a probable diagnosis of intestinal perforation in typhoid fever was made and operation advised. There are no notes as to the physical signs present in the abdomen. On admission the temperature was 99.2°; pulse, 140; respirations, 26. Operation revealed a perforation of the ileum twelve inches above cæcum, the size of a lead-pencil. For days after the operation the patient would tear his dressings off in his delirium. His emaciation was extreme. Five days after operation both parotid glands became swollen and red. On May 22d the left parotid gland was incised and an ounce of pus removed. Two days later the right side was incised. On May 27th, the fourteenth day after operation, his temperature had reached normal and the pulse rate and respiration rate were also reduced. Was taking food fairly well. The following day, however, his heart suddenly became rapid, and he died in a short time. No autopsy was permitted.

This patient unquestionably recovered from his perforation, but died as the result of sepsis from suppurating bilateral parotid bubo. The pus recovered from the parotid glands in either side showed the presence of the staphylococcus pyogenes albus. No typhoid bacilli were demonstrated.

CASE L.—A. R., aged thirty-two years; colored; hospital No. 692; admitted May 29, 1904. *Perforation undiagnosed, but discovered at autopsy,* and *death* on June 6th. Admitted to ward with history of fifteen days' illness, characterized by headache, diarrhœa, fever, and delirium. His attending physician stated that he had a hemorrhage from the bowels on the tenth day of illness. Was a poorly nourished man; sordes on lips and tongue. Pulse rapid, 142; some congestion of the base of both lungs. The abdomen was soft and not tender. Urine contained a trace of albumin and a few hyalogranular casts. After admission his general condition improved, the temperature falling from 102° on the eighteenth day to 99.2° on the following day, without change in either the pulse or respiratory rate. On June 5th, however, it was noted that he became weaker. There was absolutely no variation in the temperature, pulse, or respiration other than would be expected. On the following day the respirations had reached sixty and over, and the pulse was very rapid and running. There was present no pain in the abdomen, no distention or muscle rigidity. He died on June 6th (twenty-second day) from a supposed toxæmia.

Autopsy made the same day showed the presence of a general fibrinopurulent peritonitis and acute bronchopneumonia. Thin, punctate hemorrhages were present on the surface of the intestine, and a minute perforation, the size of a pinhead,

was found in the ileum 20 cm. from the head of the cæcum. There was deep ulceration in the cæcum. There was no tendency to wall off the perforation.

This case is interesting because neither the pulse, temperature, nor respiration showed evidence of disturbance. The patient, although stuporous, failed to show symptoms such as pain, abdominal rigidity, or distress of any character. Perforation was not even thought of at the time of death. It unquestionably had been present for at least fourty-eight to sixty hours. There was no leukocyte count made and no mention made in notes of liver dulness.

CLINICAL ABSTRACT OF CASES SUPPOSED TO BE PERFORATION, BUT PROVEN OTHERWISE.

S. J., aged seven years; hospital No. 1788; admitted August 21, 1901. *Typhoid, two relapses, periostitis, suppuration of knee and thigh, supposed peritonitis; operation, no perforation*, and *death* on November 11th. In medical ward after eight days' illness, characterized with some abdominal pain. The belly was tympanitic, tense but not tender. A few spots were present. The fever dropped after four days duration and convalescence seemed established. A relapse with much higher temperature began on the twentieth day, with acute symptoms, with fall and convalescence by the thirty-second day. During the following month there were irregular jumps in temperature until the second relapse developed on the seventieth day of his illness. During this interval the right thigh and knee had become very tender, swollen, and extremely painful, and finally developed into a large abscess of the thigh and knee-joint, which was opened and drained by Dr. Le Conte on November 4th. Coverslip smears of the pus secured showed that only streptococcus was present. On November 11th (the eighty-eighth day of illness) the belly became distended, painful, with dulness in the right flank, and costal respiration was present. The leukocytes were 1800. The stools after the development of pain showed no blood. No change in the temperature was present. Consultation by Drs. Stengel and Le Conte, who diagnosed perforation. Operation by Dr. Le Conte at 2.30 P.M. No perforation found and no cause was assigned for the symptoms present. The patient died at 8 P.M. the same night.

This case is of interest from a dual standpoint: First, the absence of a leukocytosis during the development of severe suppurative process in the thigh and knee. The leukocytes during this interval were frequently counted and at no time were found to be over 1600. The differential count showed that characteristic of a typhoid infection, considerable reduction in the polynuclear cells, 59.2 per cent. with 26.4 per cent. of small lymphocytes. When suppuration was evident in the thigh the leukocytes numbered 2850, and at the time of supposed perforation there were but 1800. No autopsy.

A. S., aged thirty-three years; hospital No. 2876; admitted December 2, 1902. *Typhoid fever, supposed perforation, no operation, recovery*, and *relapse*. Discharged January 30th. Admitted to medical ward on eighteenth day of typhoid, which was characterized by fever, chilly sensations, much sweating, and constipation. He had no abdominal pain. On admission the temperature ran about 103°, and the abdomen was flat and not tender. He complained on December 6th, at 9.45 A.M., the twenty-third day, of constant abdominal pain, especially in both lower zones, preceded by chilly sensations. The nurse stated that he had so complained for several days. He was tender on both sides below the umbilicus and the right rectus was a little rigid. At 11.30 A.M. the signs were localized to the right lower quadrant. Tenderness and rigidity were quite marked, and pain was severe. He groaned and looked much distressed in the face. The leukocytes were 8600 and showed a slight polynuclear excess, 82 per cent. The small lymphocytes, 3 per cent.; large lymphocytes, 8 per cent. At 11 P.M., the general condition was much the same; tenderness still diffuse, but most marked over the right iliac region. No liver dulness was present below the sixth rib in midclavicular line, and there was an elevated sausage-shaped tympanitic area just above and parallel to Poupart's ligament on the right It was evidently distended bowel. He lay almost constantly on his face and the pain persisted; he vomited all food. He had four greenish liquid stools containing mucus before 6.30 P.M. of this day (December 6th). The following morning the pain and tenderness were less, though still marked in the right lower quadrant, where there was still localized fulness. The leukocytes were 9200. Consultation between Drs. Le Conte, Meigs, and Harte, at 12 noon on December 6th, resulted in a diagnosis of perforation, but operation was refused. As before stated the patient improved on the following day, and on the second day after supposed perforation there was still some nausea and retching, but no vomiting. Leukocytes 8600. By December 10th the twenty-sixth day, the belly was soft, neither tender nor distended. In a few days more he seemed convalescent, but on the thirty-first day a true relapse began, lasting until the fifty-first day, with twenty days of fever. He made a good convalescence. There was no change in the pulse in this case. Study of the temperature was as follows: 6 A.M., temperature, 101.1°; pulse, 80; respirations, 28; 9 A.M., temperature, 104.3°; pulse, 100; respirations, 28; 9.30 A.M., temperature, 103.1°; pulse, 86; respirations, 38; 12.30 P.M., temperature, 104.1°; pulse, 96; respirations, 34; 3.30 P.M.

S. S., aged twenty-eight years; hospital No. 3651; admitted February 5, 1903. *Healed perforation without operation, subsequent death*. Discharged March 4, 1903, and died some five or six days later. Admitted after two weeks' illness, during which time he had headache and bronchitis and chilly sensations. Had been in bed five days before admission. Several days before this began to vomit blue and greenish material mixed with milk, which he attributed to some purgative medicine he had taken. On admission the belly was tympanitic, with slight tenderness in the right and left iliac

regions. The left half of abdomen was softer and less rigid than the right. The liver dulness was obliterated. There was no sweating and no evidence of pain in face. Perforation was, however, diagnosed and operation suggested but refused. The following day he was decidedly better, less tympanitic, and after a rather eccentric run of temperature was considered convalescent. During his convalescence he had some abdominal distention, with distinct dimpling of the abdominal wall above the umbilicus. It was thought that probably this might be due to an adherent coil of intestine. He was discharged on the forty-second day of his illness for insubordination, having been discovered in the act of consuming an entire bag of crackers. He was removed to his own home, where he was subsequently seen about five days later by the resident ambulance surgeon, at which time he had all the evidence of a general peritonitis, with which he died. After a meal of unusual proportions he had developed sudden abdominal pain, with collapse.

My impression of this case is that the man had a primary perforation which was closed in some manner, and that his subsequent indiscretion in diet before he was fully convalescent produced secondary rupture, with peritonitis and death.

B. S., aged fourteen years; hospital No. 4336; admitted March 26, 1903. *Typhoid fever, appendicitis, operation, pneumonia,* and *death* on April 13, 1903. Admitted to the medical ward on the eleventh day of typhoid, in which he had a great deal of abdominal pain. He was a mouth-breather, and after admission complained of some tenderness on left side of belly below the umbilicus. On March 28th and 29th the patient complained of severe general abdominal pain and great tenderness. There was no rigidity, but some distention. On the thirtieth day he was much improved and without pain, while again on the thirty-first the pain, with distention, returned; the right rectus was rigid; tenderness was general, but most marked in the right iliac region. Drs. Meigs and Gibbon in consultation. Diagnosis, perforative peritonitis; operation; small amount of fluid in peritoneal cavity; no perforation found, but a congested appendix with a large, firm concretion in the tip was discovered and removed. He was again transferred, after one week in the surgical ward, to the medical ward. By this time evidences of a consolidation of the middle and lower lobes of the right lung appeared. On April 12th the wound suddenly burst open in its entire length, the intestines protruded, and the patient died on the following day. In this case the temperature chart shows nothing at time of peritonitis, the fever running along about 103°. The appendicitis occurred about the thirteenth to the sixteenth day; operation on the seventeenth day of his illness.

A. A., aged twenty-eight years; hospital No. 138; admitted April 4, 1903. *Perforation diagnosed, operation, no perforation found, pneumonia, recovery.* Discharged May 25th. Admitted to the medical ward on the fourteenth day of typhoid fever, though he worked until two days before his admission. The abdomen was soft and not tender; temperature about 103.1°. The day after admission he complained of abdominal pain; abdomen was rigid and tympanitic, but relief was obtained by the rectal tube. On April 8th he had two bloody stools, and after a week the fever began to remit, while his abdomen became painless and soft. On April 10th there was evidence of rough breathing at both bases, with fine rales, and he complained of sharp pain over the left base on deep inspiration or cough. One week later the temperature touched normal, though he still complained now and then of chest pain. On April 19th (the thirty-sixth day) the temperature rose suddenly, and he had severe pain over the costal region, where an occasional friction rub could be detected. The following morning the expression was anxious, the abdomen was very rigid but not tender. There was no vomiting and the temperature was not altered. Consultation by Drs. Charles Hart and W. B. Hopkins; diagnosis, perforation. Operation by Dr. Mitchell at noon; no perforation or peritonitis found. No pain was experienced after operation for four or five days. Distinct signs of consolidation of the left base subsequently appeared. The patient made a good recovery. No temperature chart is attached to this case; there is no mention of liver dulness or special abdominal symptoms.

C. H., aged twenty-three years; colored; hospital No. 656; admitted on May 25, 1903. *Typhoid fever, suspected perforation, operation, no perforation found, recovery.* Discharged August 14th. Entered the medical ward on the tenth day of typhoid, characterized by fever and pain in back and abdomen. Was a case of moderate severity; temperature running at 103° and lower. The belly was not painful or tender. Widal was at once positive; leukocytes 2200. In the early morning on the sixteenth day he had an intestinal hemorrhage, and again on the twentieth day. On June 5th he had several enormous hemorrhages, with signs of severe shock. He was pulseless, with a temperature of 97°. Sixteen ounces of blood could be measured, and a basin of blood clots were removed from the bed. Two days after these hemorrhages there was abdominal distention, but no pain or rigidity was noted. The day following the hemorrhage the blood count was: whites, 2,660,000; leukocytes, 6700; hæmoglobin, 55 per cent. On June 10th, at 10 A.M., the abdomen was noted distended, with rigid recti, especially below the umbilical level. There was no pain present. At 12.30 P.M., however (the twenty-sixth day), he complained of severe pain in the right iliac region, with tenderness. There was no change in the temperature or pulse. The bowels were constipated at this time. Consultation by Drs. Lewis and Harte. Diagnosis, perforation. Operation by Dr. Harte showed no evidence of peritonitis and no perforation. The wound was closed and the patient made a good convalescence. Nineteen days after operation, or the forty-fourth day of his illness, the temperature was down to stay, and convalescence fully established. No cause was discovered for the symptoms.

H. G., aged twelve years; hospital No. 967; admitted on June 27, 1903. *Suspected perforation, operation, no perforation, relapse, recovery.* When admitted, on the 5th day of the disease, had a typhoid of mild severity. A loud systolic murmur was present at the cardiac apex, with left-sided hypertrophy. On July 1st, the ninth day of his illness, he complained of pain in the right iliac region, with general abdominal tenderness. Next day cried out with pain on superficial touch of the abdomen. Leukocytes 15,800. Liver dulness was present, belly was retracted. Drs. Harte and Scott agreed on operation, although no change in the pulse, respiratory rate, or facial expression was to be noted. Upon operation no perforation, no peritonitis, or cholecystitis was found, and the appendix was normal. On July 12th, ten days after operation, the following note was made by the resident physician: "For the past few days signs of consolidation and some moist rales are heard at the left base." Temperature ran a typical course, slowly falling during the last ten days, and by the twenty-ninth day remained down. He had a true mild relapse from the thirty-sixth to the fiftieth day. In this case the pain may have been due to the pulmonary consolidation, though its late appearance makes it seem doubtful. No other cause was discovered to account for it.

D. I., aged thirty years; hospital No. 3641; admitted February 26, 1904. *Operation, no perforation,* and *died* March 19th. Entered the hospital with history of having been sick with fever and headache for thirty days. He was very sick, stuporous much of the time, with poor, rapid pulse. On March 12th he was given one pint of salt solution in the right side of the abdomen by the resident physician at 3 P.M. At 8 P.M. he had severe right-sided tenderness. At 11.30 P.M. was in marked stupor, with the right leg drawn up. Belly was not distended, and there was no undue change in the pulse or respiration. Liver dulness was present. There was exquisite pain on the slightest touch upon the right side in the region corresponding to area where the hypodermoclysis was given. There was no difference in the recti. The leukocyte count at midnight was 5500. Deep pressure on the right side caused no pain. On consultation between the chief resident physician and Dr. Hutchinson, who had no knowledge of the site of hypodermoclysis, a diagnosis of perforation was made, and operation was done at 2 A.M. There was no abdominal rigidity under ether. Upon opening the abdomen no perforation was found. The man died six days subsequently, March 19th, from toxæmia. The autopsy showed active Zenker's degeneration of the abdominal muscle in the neighborhood of the place where hypodermoclysis was given. There was no perforation of the bowel present.

J. N., aged nineteen years; hospital No. 4329 (new No. 101); admitted April 22, 1904. On admission to the hospital he was sick with mild typhoid, with splenic enlargement, without distention or abdominal pain. The urine showed hyalogranular casts from the start. On the twenty-first day of his illness, at 5 P.M., he was seized with sudden and severe abdominal pain, chiefly below umbilicus. There was no special localization. The pain was severe for one hour, then became less. At 5 P. M. his temperature was 99°; at 5.20 P.M., 101°; at 8 P.M., 104.1°. The pulse rose from 80 to 120. The abdomen was not rigid, but the left rectus was slightly so. Bowels were moved at 4.45 P.M., and he vomited greenish fluid and milk at 6.30 P.M. At 11.30 P.M. he had a second attack of similar pain, when the left rectus became quite rigid. There was no abdominal distention and no localization of pain. He was quiet, however, after this, but slept little, and during the early morning hours had a profuse sweat and fall of temperature, from 104° to 99° by 4 A.M. On the following morning he had but little pain, but was distinctly tender in both lower zones, perhaps more so on the left, with rigidity of both recti, especially the left. Liver dulness was present but diminished. Consultation of surgeons and physicians at this time showed some difference of opinion, but the general impression was that peritonitis was present. The pulse and respiration had again fallen with the fall of temperature. He went on from this time without pain, but with some slight evidence of irritability of the bladder and inability to pass urine. Upon being fed he had a true relapse from the twenty-seventh to the forty-sixth day, during which time he had an acute severe cystitis. He finally recovered, with tardy convalescence. This was probably a case of acute gastric disturbance, with probably subacute cystitis.

M. S., aged thirteen years; hospital No. 738; admitted June 2, 1904, on the seventh day of what seemed a moderately severe attack of typhoid fever. Five days after admission he had a very painful sore throat. There was little or no delirium(?), nor was he much prostrated. His illness was characterized by extreme drowsiness, with some symptoms of meningitis during the second week. Kernig's sign was present. On June 21st he was considered convalescent, and was fed with a soft-boiled egg. On that day he had general abdominal pain, with no rigidity, however. On the following day there was slight abdominal distention, and for the two following days he seemed in excellent condition. On June 26th, at 5.30 P.M., he had sharp pain in the abdomen, which was not localized, and on the following morning slight distention, with some feeling of resistance and tenderness, especially marked in the left lower abdomen. On the following day he had less pain and but faint or no rigidity. At 8 P.M. (the thirty-fourth day) he had a sudden attack of abdominal pain and fall in temperature and no change in the pulse. At 9 P.M., temperature, 97°; pulse, 72; respirations, 24. 12 P.M., temperature, 99°; pulse, 128; respirations, 32. 11 P.M., temperature, 98°; pulse 100; respirations, 24. 1 A.M., temperature, 100°; pulse, 136; respirations, 40. 2 A.M., temperature, 101°; pulse, 132; respirations, 36. 3 A.M., temperature 101°; pulse, 132; respiration, 32. There was no distention; liver dulness was present. He had a second sharp attack of

pain at 11 A.M., with rigid recti, face agonized, color very poor. He had chilly sensations. At 12 noon he seemed considerably improved and almost ready to go to sleep. After 9 P.M., temperature, pulse, and respiration rose. He was seen by Dr. Lewis at 12 midnight, and at 1 A.M., when a diagnosis of perforative peritonitis was made. He was operated upon at 3.30 A.M. by Dr. Stewart, who found a large half-inch perforation in the tip of the appendix, subsequently shown not due to the presence of deep-seated ulceration. A circumscribed area of necrosis was present in the ilium when the tip of the appendix touched the gut, a true post-typhoidal appendicitis. No hemorrhage was present during this illness. No leukocyte count was made. The condition of the bowels was satisfactory at the time of the appendicitis, which is supposed to have occurred on the thirty-fourth day.

THE PROCEEDINGS OF THE SOCIETY OF NORMAL AND PATHOLOGICAL PHYSIOLOGY, UNIVERSITY OF PENNSYLVANIA.

Meeting of February 20, 1905.

A Preliminary Report upon the Systemic Action of Potassium Sulphocyanide.

Dr. Edward Lodholz.

The communication included a consideration of the influence of this salt, which is a normal constituent of the saliva upon metabolism, and also of its pharmacological action.

Upon the Influence of Copious Water Drinking.

Dr. P. B. Hawk.

A series of metabolism experiments in which a study of the nitrogen, sulphur, and phosphorus exeretions was made. This communication appeared in a previous number of the University Medical Bulletin.

Studies on the Bactericidal Action of Copper on Organisms in Water.

Dr. N. Gildersleeve.

The investigations of Moore and Kellerman on the employment of copper for the destruction of algæ have developed an excellent method for the destruction of these cryptogams, and also been the cause of a great deal of controversy over the question of employing copper for the destruction of bacteria in water. The question must be considered from the following standpoints:

1. Are bacteria destroyed by very dilute solutions of copper salts or by copper in any form?
2. Which of the salts is most active, and at the same time cheap enough to prevent the question of expense being so great a factor as to exclude its use?
3. What influence would organic and inorganic substances in the water have on the action of the copper?
4. Would the constant ingestion of small amounts of copper have a detrimental effect on the health of an individual using water so treated?

The investigation reported in this communication was undertaken to determine to what extent various bacteria are destroyed by dilute solutions of copper salts; and also to show which of these salts has the greatest bactericidal action.

In the experiments the sulphate, chloride, acetate, and nitrate were employed in solution of 1:250,000, 1:500,000, 1:1,000,000, 1:1,500,000, 1:2,000,000, in both tap and distilled water. Colloidal solutions were also employed.

The results obtained seem to warrant the following conclusions:

1. Dilute solutions of copper salts have a marked destructive action on many bacteria. Of these salts the sulphate is most active. This is probably due to the fact that it undergoes electrolytic dissociation more readily than the others.
2. The amount of sulphate to be used in the water should be from 1:250,000 to 1:100,000, depending on the character of the water.
3. Colloidal copper will quickly destroy certain bacteria; should copper vessels or plates be used to destroy bacteria in water, they must be kept highly polished or the bactericidal properties will be greatly reduced.
4. We have been unable to find evidence of copper, ingested in small quantities for long periods, having a detrimental action on the health of an individual.

Meeting of March 6, 1905.

Discussion upon the Clinical Data Obtained from Estimations of Blood Pressure.

Prof. Alfred Stengel.

Dr. Stengel, speaking regarding the clinical uses of determinations of the blood pressure, called attention to the fact that estimations of arterial tension can be of value only when the maximum and minimum tensions are separately recorded. An attempt to draw deductions from the observations of the maximum or minimum alone would lead to erroneous conclusions. Thus in a case of aortic regurgitation it will be found that the systolic pressure is uniformly high, which might suggest exceptional efficiency of circulation. When, however, the diastolic pressure is recorded with the systolic, it is found that the fluctuation is so great that the average pressure is below the normal. Similarly in cases of arteriosclerosis, it is sometimes found that the systolic pressure is low, which might be found to indicate a marked falling off in the mean pressure, whereas the maintenance of a high diastolic pressure evidences the indications of the average. The speaker has found the Stanton apparatus useful in clinical work and has found it advantageous in studying cardiovascular conditions, especially arteriosclerosis and in the management of cases of nephritis. In all clinical work it must be recalled that the data obtained are approximate only, a certain range of errors must be expected, on account of deficiencies in the apparatus and anatomical or other peculiarities in the patient.

Demonstration of Apparatus for Determining Blood Pressure in Man.

Dr. W. B. Stanton.

Dr. H. C. Wood, Jr., spoke on the "Sphygmomanometer in Therapeutics." He believed that very frequently the dose of drugs employed, especially in circulatory conditions, was too small. It is necessary to give sufficient quantities to produce an effect. The only way we have had of judging whether the amount given had any effect is by the physiological limit. The physiological limit is an accidental symptom and often has no direct relation to the desired action. For example, the physiological limit for strychnine is twitching of the muscles; it is quite plausible that strychnine might stimulate the spinal cord before it had affected the vasomotor centres, or *vice versa*. Again, the physiological limit for veratrum viride was slowing of the pulse; slowing of the pulse is produced by the alkaloid rubijervine, whereas it is jervine which produces the lowering of the blood pressure. The sphygmomanometer, therefore, had a very useful place in the gaining of information as to the effect of treatment upon the circulation.

Some Experimental Observations upon the Lower Animals to Determine the Accuracy of Stanton's Apparatus in Recording the Maximum and Minimum Blood Pressure.

Dr. D. M. Hoyt.

Appears in this number of the University Medical Bulletin.

POST-GRADUATE COURSE

DEPARTMENT OF MEDICINE

UNIVERSITY OF PENNSYLVANIA

COURSES OFFERED TO GRADUATES IN MEDICINE DURING THE MONTHS OF MAY AND JUNE, 1905

ANNOUNCEMENT

The course will extend over a period not exceeding six weeks.

Beginning May 15, 1905, the University will conduct a spring course in Medicine, designed especially for practitioners, but open also, in the laboratory courses, to advanced students in Medicine. It embraces almost the entire curriculum of Medicine, and has been devised to meet the requirements of a wide group of practitioners and students of Medicine.

In designing the instruction offered in the spring course, the needs of the practitioner have been kept in view, and so far as possible the work has been made of purely practical character. While this feature is emphasized in the clinical branches and specialties, it has not been lost sight of in the laboratories. In all the courses the work is of a nature to appeal to the surgeon and general practitioner who wish to revive or complete their knowledge of certain subjects, and to advanced students in Medicine who may not have had opportunities to pursue these courses of study.

The number of attendants upon certain clinical courses will be necessarily limited, in order that close personal attention may be accorded the patients. This number will vary with the nature of the course; and the admission, under these circumstances, will be made in the order of application.

The schedule of hours for post-graduate study is so arranged that a comprehensive course may be taken without conflict of hours, and for this purpose the subjects have been divided into two groups·

Group I. is devoted entirely to Internal Medicine, including laboratory and clinical work, and to the following specialties: Pediatrics Neurology, Ophthalmology, Otology, Rhinology, and Laryngology.

Group II. is devoted entirely to General Surgery, including Surgical Anatomy and Pathology, and to Gynecology, Obstetrics, Orthopedic Surgery, Genitourinary Diseases, and Dermatology

To those, however, who are desirous of devoting more time than is allotted on the schedule to any one subject, special courses and opportunities are offered for more advanced work.

LECTURE SERIES

MEDICINE

1. Medical Clinic. Dr. Tyson, in the Medical Amphitheatre, University Hospital, Saturdays at 9. A.M.

2. Medical Clinic, or Bedside Instruction. Dr. Musser, University Hospital, Thursdays at 12 noon

3. Medical Clinic, or Bedside Instruction. Dr. Stengel, University Hospital, Mondays at 12 noon.

4. Clinical Medicine. Dr. Fussell, in the Out-patient Department of the University Hospital, Thursdays at 1 P.M.

5. Clinical Medicine, with Especial Reference to Physical Diagnosis. Dr. Sailer, at the Philadelphia Hospital, Tuesdays, Wednesdays, and Fridays at 12 noon.

6. Clinical Medicine, with Especial Reference to the Diagnosis and Treatment of Diseases of the Gastrointestinal System Dr. Steele, University Hospital, Mondays at 1 P.M., and Saturdays at 12 noon.

7. Clinical Medicine, with Especial Reference to the Diagnosis and Treatment of Cardiovascular Diseases. Dr. Herman B. Allyn, at the Philadelphia Hospital, on Tuesdays, Wednesdays, and Fridays at 1 P.M.

8. Clinical Laboratory Methods. A course including Methods of Examining the Blood, Sputum, Urine, and Stomach Contents, to be given by Dr. William Pepper, at the William Pepper Clinical Laboratory, daily, from 11 A.M. to 12 noon, throughout the course.

9. The Treatment of Pulmonary Tuberculosis. Dr. W. B. Stanton, in the Pavilions for Tuberculosis of the Philadelphia Hospital, two afternoons a week.

PEDIATRICS

1. Clinical Instruction in the Diseases of Children. Drs. Griffith and Ostheimer, in the Wards of the University Hospital, on Wednesdays at 4 P.M., throughout the course.

2. Feeding in Infancy. Dr. Thompson S. Westcott, on Mondays and Fridays, in the Amphitheatre of the Children's Hospital, from 4.15 to 5.15 P.M., throughout the course.

This course will include the Modification of Milk. The Calculation of Percentage Formulæ. General Considerations of Substitute Feeding. Practical Application of Percentage Feeding. Weaning. Feeding in Difficult Cases. Dietetic Treatment of the Chronic Gastrointestinal Catarrhs. Various Expedients Necessary in Special Cases. Differential Modifications of Proteids, etc. Use of Cereal Preparations, Condensed Milk, etc. Clinical Cases Illustrating Nutritional Diseases: Rickets, Scurvy, Atrophy, Tuberculosis, Syphilis, and their Dietetic Management.

SURGERY

1. Clinical Surgery. University Hospital, daily at 1 P.M., including operations in the Surgical Clinic, Surgical Diagnosis, Ward Rounds, and Demonstrations of the Modern Methods of Administering Anæsthetics.

2. Surgical Pathology. Dr. Müller, Tuesdays and Thursdays, from 11 A.M. to 1 P.M., at the New Medical Laboratories. This course consists in the demonstrations of the gross and microscopic lesions of the more common surgical affections, in so far as they apply to diagnosis and treatment.

3. Operative Surgery on Cadavers and Animals. Dr. Carnett. Mondays and Fridays, 11 A.M. to 1 P.M. This course will include Intra-abdominal Operations upon Animals (operations upon the Stomach, Gall-bladder, and Intestines), and such operations upon the Cadaver as cannot be demonstrated to advantage upon the Living Animal. The course will be arranged in accordance with the special needs of the Student. (Limited to ten.)

4. Surgical Anatomy. Dr. Davis. Mondays and Fridays, 2 to 3 P.M., Logan Hall. With especial reference to the anatomy of the peritoneal cavity, of fractures and dislocations, including demonstrations of methods of reducing dislocations.

5. Skiagraphy, Radiotherapy, and Phototherapy. Dr. Pancoast. Mondays, Wednesdays, and Fridays, 9 to 11 A.M. *X*-ray Department, University Hospital. Preliminary instruction in the various parts of an *x*-ray equipment, the handling of the apparatus, and in the principles of electric currents used in the production of the *x*-rays. This will include also the dangers in their application, their effects upon healthy and diseased tissues, and the methods of protection to the patient and operator. Instruction in the technique of radiographic exposures and the development of plates in the dark room. The therapeutic application of *x*-rays, with technique required for treating various pathological conditions, with demonstrations by treatment of patients. The therapeutic use of Finsen rays and "High Frequency Currents."

6. Orthopedic Surgery. Orthopedic Clinic, Dr. Willard, Tuesdays, 12 to 1; Drs. Young, Spellissy, and Reed, Mondays, Thursdays, and Fridays, 12 to 1; Operations, Lectures, Demonstrations, and Practical Work in the Orthopedic Ward and Dispensary. The Special Orthopedic Gymnasium for the Treatment of Paralyses, Deformities, Curvatures, etc., is open daily from 12 to 2.

7. Pediatric Surgery. Dr. Jopson. Wednesdays and Saturdays, Children's Hospital, 11 A.M. to 1 P.M.

8. Genitourinary Diseases. Drs. Neilson and Siter. In the Out-patient Department of the University Hospital, Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1. This course is altogether practical, and covers the following subjects: Venereal Diseases, Surgical Diseases of the Genitourinary Organs, the Use of Instruments for Diagnosis and Treatment of Diseases of the Urethra and Bladder, and demonstration of operative procedures.

9. Minor Surgery. Dr. Norris, University Hospital, daily from 12 to 1 P.M.

GYNECOLOGY

1. Gynecological Clinic. Dr. Clark. Wednesdays and Fridays, 2 to 4 P.M., University Hospital. The practical work in this course will be limited to five graduate students.

2. Gynecological Clinic. Dr. Beyea Tuesdays and Thursdays, 11 A.M. to 1 P.M., Gynecean Hospital.

3. Gynecological Pathology Dr. Anspach. Hours to be arranged for the convenience of those taking the course. (Limited to ten.)

OBSTETRICS

Dr. Hirst and assistants. Tuesdays and Thursdays, 3 to 4 P.M., in the Maternity Pavilion of the University Hospital. This course consists in demonstrations of the Surgical Treatment of the Injuries of Childbirth by Primary, Intermediate, and Secondary Operations; Treatment of the Pelvic and Abdominal Complications of the Child-bearing Process by Pelvic and Abdominal Surgery; the Obstetrical Operations, Obstetrical Diagnosis, and Preliminary Examination of the Patient, and the Management of the Puerperium.

DERMATOLOGY

Dr. Hartzell. Mondays, Tuesdays, Thursdays, and Fridays, 12 to 1 P.M. This course is given in the Out-patient Department of the University Hospital and Wards of the Philadelphia Hospital, and will be devoted to the Examination, Diagnosis, and Treatment of patients in daily attendance at the clinic.

NEUROLOGY AND PSYCHIATRY

1. Clinics. Dr. Mills on Mondays and Dr. Spiller on Tuesdays and Thursdays, 3 P.M., at the University or the Philadelphia Hospital.

2. Neuropathology. Dr. Spiller will give practical instruction either by the lantern or in the laboratory once a week for those desiring to take Neuropathology in connection with the clinical work.

3. Electrotherapeutics and Ward Class Demonstrations. At least once a week, by Dr. Potts and assistants, University Hospital.

4. Psychiatry. Dr. Burr. Instruction in Mental Diseases either by lectures or by ward class demonstrations, Wednesdays and Fridays, 3 P.M., Philadelphia Hospital.

5. Special Course. The course announced above is open to all students of the post-graduate department. Any student wishing to take Neurology and Psychiatry as a special subject, or in combination with one or two other subjects, can make arrangements with the Dean of the Faculty and the Teachers in the Neurological Department for the fuller course.

OPHTHALMOLOGY.

This course is designed for those who are especially interested in the eye, and is limited to ten.

1. Operative Clinic. Dr. de Schweinitz, Thursday, 3 to 4 p.m., University Hospital.

2. External Diseases of the Eye, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 3 to 4 p.m.

3. Operations on Animals' Eyes, Dr. de Schweinitz, assisted by Dr. Mellor, Tuesdays, 4.30 to 5.30 p.m.

4. Functional Testing of the Eye, including the principles of Refraction, Muscle-balance Testing, Retinoscopy, and Ophthalmometry. Dr. Carpenter, in the Eye Dispensary of the University Hospital, Mondays, Tuesdays, Wednesdays, and Fridays, 2 to 3 p.m.

5. Pathological Histology. Dr. Shumway, Mondays, Wednesdays, and Fridays, 4 to 6 p.m.

OTOLOGY.

Dr. Randall. (*a*) Daily Clinics at the University Hospital. (*b*) Instruction in the Anatomy of the Ear by means of lantern demonstrations and anatomical preparations in connection with the Wistar Museum of Anatomy.

In demonstrating operative procedures, it is expected that either clinical material or cadavers will be used

LARYNGOLOGY.

Dr. Grayson. Daily in the Laryngological Clinic of the University Hospital, at 2.30 p.m. A course in Instrumental Technique and in the Diagnosis and Treatment of Diseases of the Nose and Throat. The microscope will be used to supplement the clinical diagnosis of neoplasms and exudative inflammations, and in the treatment. Instruction will be given in the ordinary methods of local therapeusis, but opportunities will be offered to perform the various operations for deflection of the nasal septum, for the removal of polyps, the faucial tonsils, adenoid growths, etc.

Note.—Those desiring to take the course in both Otology and Laryngology may take these subjects on alternate days.

BACTERIOLOGY AND HYGIENE

1. Elementary Bacteriology. Drs. Gildersleeve, daily, 9 to 11 a.m., in the Laboratory of Hygiene. This course is designed to supply the needs of the practitioner of medicine. It comprehends the preparation of culture media, the methods of sterilization, the methods of isolation and study of bacteria in pure culture, the study of the best known and most important of the pathogenic species, the methods of disinfection, the use of the microscope, and the methods of staining employed in bacteriological work.

2. Advanced Work in Bacteriology. Dr. Bergey, daily, 9 to 11 a.m., in the Laboratory of Hygiene. This course will be arranged in accordance with the qualifications and inclinations of each individual student.

3. Practical Hygiene. Dr. Bergey, 9 to 11 a.m., daily, in the Laboratory of Hygiene. Applicants for the course must possess a working knowledge of quantitative chemical analysis. The course covers exercises in the physical and chemical study of the atmosphere, with methods of recording results; studies in ventilation and heating, and methods for estimating extent of the same; physical, chemical, and bacteriological study of water; the artificial and natural methods of water purification; pollutions to which water is liable; interpretation of results of analysis; studies of milk from the sanitary standpoint; sanitary food inspection and analysis.

CHEMISTRY

1. Analysis of the Urine. Drs. Marshall, D. W. Fetterolf, Ryan, and Hawk. Tuesdays and Thursdays, 9 to 11 a.m., Robert Hare Chemical Laboratory.

2. Toxicology. Tuesdays and Thursdays, 9 to 11 a.m., Robert Hare Chemical Laboratory.

3. Elementary Physiological Chemistry. This course will consist of a systematic study of the carbohydrates, fats, proteids; salivary, gastric, and pancreatic digestions, and of the bile, milk, and blood. If desired, work will be given in tissue chemistry and in general food analysis. (This course will only be given in the event of there being at least six students.)

ANATOMY

1. Embryology. Dr. Piersol. Tuesdays, Thursdays, Saturdays, 9 to 11 a.m., Logan Hall. 2. Microscopic Technique. Drs. Piersol and Formad. 3. Practical Anatomy. Dr. G. Fetterolf.

PATHOLOGY

Drs. Smith, Loeb, and C. A. Alburger. 1. Autopsy-making. 2. Selected Experimental Pathology. 3. Elementary Pathological Histology. 4. Advanced Pathological Histology. New Medical Laboratories. (This course will not be given to classes of less than six.)

PHYSIOLOGY

Drs. Reichert and Lodholz. 1. Elementary Course in Practical Physiology. 2. Advanced Course in Practical Physiology. (These courses will not be given to classes of less than six.) Hours to be arranged to suit the convenience of those taking the courses. New Medical Laboratories.

For further particulars apply to

Dr. CHARLES H. FRAZIER, Dean,

Thirty-sixth Street and Hamilton Walk, Philadelphia, Pa.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. I of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

Horatio C. Wood, M.D., LL.D., Professor of Materia Medica, Pharmacy, and General Therapeutics.

Edward T. Reichert, M.D., Professor of Physiology.

Barton Cooke Hirst, M.D., Professor of Obstetrics.

J. William White, M.D., John Rhea Barton Professor of Surgery.

George A. Piersol, M.D., Professor of Anatomy.

John Marshall, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology.

Louis A. Duhring, M.D., Professor of Dermatology.

Alexander C. Abbott, M.D., Pepper Professor of Hygiene and Bacteriology.

John G. Clark, M.D., Professor of Gynecology.

George E. de Schweinitz, M.D., Professor of Ophthalmology.

Charles H. Frazier, M.D., Professor of Clinical Surgery, and Dean of the Faculty.

Allen J. Smith, M.D., Professor of Pathology.

De Forest Willard, M.D., Professor of Orthopedic Surgery.

B. Alexander Randall, M.D., Clinical Professor of Diseases of the Ear.

J. P. Crozer Griffith, M.D., Clinical Professor of Diseases of Children.

John H. Musser, M.D., Professor of Clinical Medicine.

Alfred Stengel, M.D., Professor of Clinical Medicine.

Gwilym G. Davis, M.D., M.R.C.S. Eng., Associate Professor of Applied Anatomy.

Edward Martin, M.D., Professor of Clinical Surgery.

Thomas R. Neilson, M.D., Clinical Professor of Genitourinary Diseases.

Charles K. Mills, M.D., Professor of Neurology.

William G. Spiller, M.D., Professor of Neuropathology and Associate Professor of Neurology.

Charles W. Burr, M.D., Professor of Mental Diseases.

M. Howard Fussell, M.D., Assistant Professor of Medicine.

Charles P. Grayson, M.D., Clinical Professor of Laryngology and Rhinology.

Adolph W. Miller, M.D., Assistant Professor of Materia Medica.

Alfred C. Wood, M.D., Assistant Professor of Surgery.

Richard C. Norris, M.D., Assistant Professor of Obstetrics.

David H. Bergey, M.D., Assistant Professor of Bacteriology.

Richard H. L. Harte, M.D., Adjunct Professor of Surgery.

J. Alison Scott, M.D., Adjunct Professor of Medicine.

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AND

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HISTORY AND LITERATURE.

The subject to which attention will be directed in the present communication is of continuing interest to the physiologist, neurologist, and surgeon. It first claimed particular attention through the suggestions based upon clinicopathological observations of Hughlings Jackson, and the physiological researches of Hitzig and Fritsch, and of Ferrier. While a *résumé* of the history of the subject would be of much value, such a historical summary would divert interest from the practical matters which it is our particular design to emphasize. We shall, therefore, pass at once to a consideration of our subject as designated in the title of this paper, and shall try to strictly limit ourselves to the points indicated by that title.

The first electric investigations of the human brain were made by Bartholow.[1]

The patient, a woman aged thirty years, had an epithelioma of the scalp which had destroyed the bone and exposed the dura. Experiments were made with both the faradic and galvanic currents with insulated needle electrodes, which were applied to the dura and also passed into the substance of the brain. Decided results were obtained from the dura and the cerebral stimulation. These were not of a character to indicate the position of separate motor centres. The method of investigation used by Bartholow was much criticized, and he afterward expressed regret at having employed it. It was objectionable in that the needles were inserted into the brain substance, and this in the days when antiseptic and aseptic precautions were not commonly used.

The early contributions to our knowledge of faradization of the human cortex were chiefly made by American neurologists and surgeons, and the observations of our countrymen have continued to hold first place in this field of practical research.

In 1897 Lamacq,[2] of Bordeaux, published a valuable paper on the cortical motor centres of the human brain, as determined by faradic excitation of the cerebral hemispheres of man.

This paper has not as yet been followed by any other of the same scope and importance. Lamacq collected chiefly from American and English medical literature the recorded observations up to the time of the appearance of his contribution, and, in addition, included a series of unpublished notes of cases furnished to him by Dr. W. W. Keen. The previously recorded cases summarized and reviewed by him included observations by Bartholow, Sciamanna, Horsley, Keen, Lloyd and Deaver, Mills and Hearn, Nanerede, Kammerer, Mills and Keen, Ransom, Sachs and Gerster, Steiglitz, Warnots, Laycock, Diller and Buchanan, Parker and Goteh, Vierordt and Schlesinger.

Lamacq also reviews observations bearing upon the subject by Starr, Angell, Bidwell and Sherrington, Dana, Guthrie, Hochenegg, Horsley, and Horsley and Beevor. For the bibliography of these investigators the reader is referred to the paper of Lamacq. Most of the contributions have been studied in the original by us, and will be used in drawing our conclusions, but it is apart from our purpose to elaborately discuss the literature of the subject.

Since the date of Lamacq's publication, contributions on the subject of human cortical faradization have been meagre, but attention should be directed to the recent articles by Krause,[1] Rothmann,[2] and Brodman.[3]

Highly important papers by Grünbaum and Sherrington,[4] recording the results of electric experimentation on the motor region of the higher apes, should be referred to in connection with the subject of cortical faradization of the brain of man. These physiologists, as is well known, hold,

[1] American Journal of the Medical Sciences, April, 1874.

[2] Arch. Clin. de Bordeaux, November and December, 1897, vol. vi.

[1] Concerning the Pathology of Jacksonian Epilepsy and its Operative Treatment; remarks at Berliner medicinische Gesellschaft, February 22, 1905, referred to in Berl. klin. Wochensch., March 6, 1905, p. 272.

[2] Berl. klin. Wochensch., January 23, 1905, p. 101.

[3] Ibid. Remarks made in the discussion of Rothmann's paper, Brodman in these remarks referring to observations made conjointly with Krause.

[4] Proceedings of the Royal Society of London, November 21, 1901; February 27, 1902, and May 25, 1903.

as the result of their experiments, that the motor region, at least in the anthropoids, is situated cephalad of the central fissure.

We shall first call attention briefly to three of the earliest cases in which cortical faradization was employed in Philadelphia, this being in 1888. They are of interest historically and also because of the striking results obtained, and are included in Lamacq's series of cases. They are the only recorded cases to which any detailed consideration will be given.

In the first case, recorded by Keen,[1] trephining and cortical excision were performed by him May 30, 1888, the position of the hand centre having been fixed by means of bipolar faradization. Three convolutions running somewhat in the direction of the central fissures were at first exposed. No response was produced when the two most posterior of these gyres were touched by the electrodes, but when they were applied to the most anterior the hand instantly moved in extension on the wrist to the mid-line and to the ulnar side at different touches, the fingers being extended and separated.

From the description, the opening in this case was first so made with a one and one-half inch trephine as to probably only expose the postcentral and precentral gyres at about their middle part. The opening was enlarged, chiefly forward and downward, till it measured two and one-half inches anteroposteriorly by two and one-quarter inches vertically. The centre pin of the trephine was placed presumably about one-eighth inch behind the central fissure and one inch above the temporal ridge. The opening extended forward one and three-eighths inches, backward one and one-eighth inches, upward one inch, and downward one and one-quarter inches. After excision of what was believed, as the result of the faradic excitation, to be the hand and wrist centres, another application of the current was made just above the excised area, with the result that movements of flexion and extension of the left elbow and of the shoulder, which was raised and abducted, were noticed.

Exciting the convolution below the excised portion, an upward movement of the whole left face occurred, no one muscle being noticeably in isolated contraction. The movements performed by the platysma and the depressors of the mouth were not called forth. Finally, movements of the hand were evoked by touching the white matter at the bottom of the excised area.

This case is worthy of special citation here because of the care with which the position of the central fissure was determined, the precision with which the faradic investigation was made, and the exact and well-defined responses which were obtained. The positions for extension of the hand at the wrist, the abduction of the hand, and the separation and extension of the fingers were obtained. Excitation of a centre above that for movements of the hand at the wrist, and of the movements of separation and extension of the fingers, caused movements of the elbow and of the shoulder, while faradization below the excised area caused an upward movement of the entire opposite side of the face. The results of the first faradic applications were re-enforced by touching the white matter at the bottom of the excised area, this causing movements of the hand. In this one well-studied and well-recorded case, the relative positions, from above downward, of the shoulder, elbow, hand, and face centres were demonstrated. The entire series of observations also indicate that the centres for the movements evoked were, in all probability, situated cephalad of the central fissure, as it will be recalled that no response was obtained when the applications were made to the two most posterior of the gyres in view.

The case of Lloyd and Deaver[1] was one of focal epilepsy, successfully treated by trephining and excision of cortical motor centres. The operation was performed June 12, 1888, by Dr. J. B. Deaver. One of us, Dr. Mills, was present at the operation. Following Reid's and Horsley's lines, an area was first exposed by an inch and a half trephine. This was supposed to be on both sides of the central fissure at about the junction of its middle and lower thirds. After the trephine opening was made the area was much enlarged, especially in an anterior direction, by a rongeur.

As it was not possible to locate the centre for excision by inspection of the convolutions, bipolar faradization was resorted to for this purpose. This was presumably begun at a point back of the central fissure, the effort being made to apply the electrodes at Ferrier's wrist centre in the postcentral gyre. The result was muscular contractions, causing turning in of the thumb on the palm, flexion of the fingers, and flexion of the wrist, extending to flexion of the elbow. Lloyd says that while the point of application was behind what appeared to him to be the Rolandic fissure, the difficulty of identifying fissures and convolutions in a small trephine wound is extraordinary. At a point farther below and in front of a fissure, probably the central, seen in the middle of the wound, faradic stimulation caused marked contraction of the face muscles of the affected side. The mouth was drawn toward the left side with a tremulous motion, and soon the tongue began to protrude toward the left corner of the mouth. Next the left thumb was adducted into the palm, then the fingers were contracted into the palm, and about the same time the face muscles began to contract more actively, while the head was drawn to the left side, and the left eyelid began to work. The hand was gradually

[1] American Journal of the Medical Sciences, October and November, 1888, vol. xcvi., n. s.

[1] American Journal of the Medical Sciences, November, 1888, vol. xcvi., n. s.

closed, and contraction of the forearm and arm began, while the latter was drawn from the side to an angle of forty-five degrees (deltoid action), and contraction of the biceps occurred. No contraction of the leg muscles occurred at any time.

The case of Mills and Hearn,[1] in which operation was performed July 28, 1888, by Dr. W. J. Hearn, was one of trephining and cortical excision. The region intended to be exposed was the lower two-thirds of the arm area, the upper anterior portion of the face area, the hinder upper part of the speech area, and a posterior strip of the area for movements of the head and eyes.[2] The convolutions uncovered were therefore presumably nearly the lower halves of the two centrals, the posterior extremity of the second frontal, and the posterior superior corner of the third frontal. Four distinct responses were obtained on careful bipolar cortical faradization: (1) in the most anterior position at which movements resulted, distinct conjugate deviation of the head to the opposite side; (2) a little behind and below this point, drawing of the mouth outward and upward; (3) about half an inch above this spot for movement of the angle of the mouth, extension of the wrist and fingers; (4) behind and above the latter point, distinct flexion of the fingers and wrist. Continuing and increasing the faradic application at this last determined point, the fingers, thumb, wrist, and forearm were successively flexed, and the whole extremity assumed the "wing-like" position, the order of events, according to three persons who were present and who observed the spasms for the relief of which the operation was done, being exactly that which had been noticed in the beginning of the patient's convulsive seizures.

A study of the above description of the opening and of the points at which applications were made shows that they were all cephalad of the central fissure. The position of the head and the eyes given in the diagram published in 1888 was in the caudal portion of the second frontal gyre at about its junction with the precentral. Starting with the application made here, a point a little below and behind this would evidently be in the precentral convolution, near the junction of its lower and middle third; a spot one inch above would still be in the precentral and a position behind and above this point probably reached only to the central fissure at the most.

Passing by the other observations collected by Lamacq, these three cases are recalled in some detail to illustrate the exact manner in which the bipolar faradization was used as early as 1888 and subsequently by Philadelphia surgeons and neurologists; and also because of their unusual value and their important bearing upon the questions of the precentral localization of the entire motor area.

We shall next give a series of hitherto unpublished observations; in the first seven cases the operations were all performed by Dr. Frazier, the cases, as indicated in the summaries, having been under the care of Drs. Mills, Spiller, or McConnell, or having been directly in the service of Dr. Frazier.

NEW OBSERVATIONS.

Observation 1. This case is reported in full by Dr. J. W. McConnell, in the issue of the University of Pennsylvania Medical Bulletin in which this article appears. The case was studied by Dr. Mills and Dr. Spiller in consultation, and the operation was performed by Dr. Frazier, May 21, 1903. The patient was a young man who had a tumor lying athwart the posterior portion of the first and second frontal convolutions.

The base of the flap was parallel to the Sylvian fissure; both its anterior and posterior boundaries were practically vertical. The opening was in front of the central fissure, except at about its lower fourth. During the progress of the operation the opening was increased in front and upward with the rongeur.

The electric applications were made over apparently uninjured cerebral substance between the posterior limit of the tumor and the posterior limit of the opening. The upper margin of the opening was one inch from the mesal line. The first application was made one and one-half inches from the upper margin of the opening and one and one-half inches anterior to its posterior margin; it caused a twitching of the upper eyelid on the right side, followed by spasm of the right face. The second application was made two-fifths of an inch above the first and gave closure of both eyelids. The third application, two-fifths of an inch below the first, gave contraction of the right upper eyelid and of both masseters; the left eyelid did not move. An application one and nine-tenths inches posterior to the anterior edge of the opening and one and one-half inches from the superior border of the opening gave contraction of the right upper eyelid and of the right masseter. The next application, made four-fifths of an inch from the anterior edge and one and one-half inches below the superior edge, gave forward movements of the head and contraction of both masseters and of both temporals.

All of these applications, with the possible exception of one, were well forward of the central fissure.

Observation 2. The patient was a boy, aged eleven years, with epilepsy, in whose case the diagnosis of dural

[1] Transactions of the Congress of American Physicians and Surgeons, 1888, vol. i.; also Brain, 1890, vol. xii. p. 273.

[2] In speaking of these areas for movements of the arm, the face, the head, the eyes, and for speech, they are of course referred to as understood at the time, and as outlined in the scheme of Dr. Mills, published in 1888. In this scheme the postcentral as well as the precentral gyre and parts anterior to it were included in the motor region.

adhesions over the motor area had been made. He was under the care of Dr. Spiller.

The operation was performed May 6, 1905, by Dr. Frazier, an osteoplastic flap being made in the usual manner. It was designed to have the opening two-thirds in front and one-third behind the central fissure. Its upper border was one-half inch from the mesal line, and was four inches in length, as measured by the incision in the scalp. The anterior and posterior heights of the flap were also about four inches. The length of the base line was two inches, and this was situated one-half inch above the line of the Sylvian fissure and parallel with it.

After the dura was raised, a fissure, apparently the central fissure, was seen at about the middle of the opening, although its identity was, of course, uncertain.

Six applications were made with the faradic current of the strength usually employed, but no response was obtained. Three of these were at different heights in the postcentral and three at different heights in the precentral gyre. The first response obtained was at the seventh application, which was made one inch below the superior and one and three-fourths inches in front of the posterior margin of the opening, and therefore unquestionably in front of the central fissure. The movements resulting were those of the jaw and an uncertain movement in the right arm. A final application, made one inch below and three-quarters of an inch in front, resulted in flexion of the right arm on the forearm and a movement in the right face.[1]

This last result was probably due to stimulation of the postcentral convolution, but a considerable faradization of the cortex had taken place before it was obtained.

Observation 3. The patient was a girl, aged seven years, who was under the care of Dr. Spiller. The diagnosis of traumatic epilepsy had been made.

The operation was performed by Dr. Frazier April 16, 1905. The usual osteoplastic flap for exposure of the motor region was made, with the view of uncovering the cortex two-thirds in front and one-third behind the central fissure. The upper limit of the incision was one-half inch from the mesal line. The length of the superior scalp incision and the length of both the anterior and posterior sides were as nearly as possible four inches. The base line, which was two and one-half inches in length, corresponded to the line of the Sylvian fissure.

Responses to the faradic applications made were obtained three times: the first was with a weak current, the electrode being applied one-half inch below and three-quarters of an inch in front; movement of the jaw resulted. A fissure, apparently the central, was visible, and the electrode, although applied three-quarters of an inch by measurement in front of the posterior bone line, was placed directly over this fissure. The second response with the same current was obtained one-half inch below and one inch in front, this causing movements of the shoulder and in the face. The current was now made somewhat stronger, and when an application was made two inches below and one-half inch in front, movements of the right shoulder and of the jaw occurred.

Observation 4. The patient was a man, aged thirty-seven years, with a diagnosis of traumatic epilepsy. The case was under the care of Dr. Spiller.

The operation was performed by Dr. Frazier March 4, 1905. The opening was made on the right side of the head. The scalp incision, which was parallel with the mesal line and one-half inch below it, was three and one-half inches in length. Each anterior and posterior boundary was three inches in height. The base line was two inches in length. The flap was made on the usual plan.

Four unipolar applications with the usual current used at the beginning of the trials gave no response, three of these being behind and one in front of the central fissure. The fifth application, which was made one-half inch in front and one inch below, caused elevation of both shoulders. Another application, one-half inch in front and one and one-half inches below, gave a similar response. Another application, one-half inch in front and two inches below, gave response in both shoulders and in the right side of the neck. The next application, one and one-fourth inches in front and one-half inch below, gave no response. The next application, one and one-fourth inches in front and one inch below, caused response in both shoulders, the right and left upper arm, and the right pectoral muscle. The succeeding applications and their results were as follows: Two inches in front and one-half inch below, response in the left and right shoulder; two inches in front and one inch below, response in the left and right shoulder; two inches in front and one and one-half inches below, response in the right shoulder, left shoulder, and left forearm.

At first we were at a loss to account for the response in both shoulders, but it may have been due to the large-sized electrode which was applied to the back, reaching to both sides of the mesal line.

Observation 5. The patient, a man aged thirty-two years, was under the care of Dr. Mills. The diagnosis of brain cyst or tumor had been made.

Dr. Frazier operated May 23, 1905, exposing the motor area with the usual flap, the upper border of the opening, three and one-half inches long, being one-half inch from the mesal line. The anterior and posterior boundaries were three inches in height and the base line two inches. The

[1] As in the other cases recorded, when the expression below and in front is made use of, it means in every instance below the upper margin and in front of the posterior margin of the opening.

operation was planned to have the opening one-third behind and two-thirds in front of the central fissure. A subcortical cyst was found in the anterior part of the opening.

Several unipolar faradic applications were made, or at least were attempted to be made, the current being gradually increased. No response was obtained, and it was found that one of the electrodes had become detached. The connection having been made, an application was made at a point just behind the central fissure, at about the middle of the opening, which resulted in a very marked response. The right arm flexed at the elbow at an angle of about 130 degrees, complete flexion at the wrist taking place almost simultaneously and immediately afterward flexion of the fingers. This was followed by twitching or clonic spasms of the entire upper extremity, the parts of the limb being retained in the position above described. The spasm in the right arm was followed by some twitchings in the leg and face of the same side, and eventually by a spasm in the left upper extremity, the left forearm being flexed on the arm at nearly a right angle.

This case is presented to indicate that a strong current applied even behind the central fissure may cause convulsive response, which, beginning in the parts controlled by the centres nearest the electrode, may extend to other portions of the same side of the body or even to the opposite side. It is probable that the extension of the opposite half of the body is brought about by way of the bulbar or spinal commissures.

Observation 6. The patient was a girl aged nine years. The diagnosis of adhesions over the face area was made. The case was under the care of Dr. Spiller.

The operation was performed March 31, 1905, by Dr. Frazier, the opening being made on the left side of the head with the usual osteoplastic flap, the scalp incision being one-half inch from the mesal line.

This case is recorded simply as showing that unipolar cortical faradization sometimes results negatively. Six applications of the current, usually producing some response, were made equally in front and behind the central fissure. A much stronger current was applied with the same negative results. The conditions were the same as in the preceding cases.

Observation 7. The patient was a boy, aged fourteen years, who had been shot in the left temple, and was under the care of Dr. Frazier. At the time of admission to the hospital his main symptoms were impairment of muscular and cutaneous sensibility, astereognosis, etc., in the right upper extremities, indicating a probable lesion of the postparietal region, where the position of the bullet was fixed by the *x*-rays.

The operation was performed March 17, 1905. The opening, somewhat irregular in shape, was two and three-quarter inches in its superior limit or length and two and three-eighths inches in height. It was chiefly posterior to the central fissure, but included portions of the leg and arm centres of the precentral convolution. The bullet was not found.

A series of faradic applications were made to the cortex posterior to the central fissure without any response. The strength of the current was increased until it was as great as that employed in the other observations here recorded.

This case is recorded to show that faradic applications made over the postcentral and the superior and inferior parietal convolutions when the precentral area was unstimulated did not cause response in movement.

For the three following observations we are indebted to Dr. W. W. Keen, who has kindly furnished us with the notes of the cases, these not having been previously published.

Observation 8. The patient was a young woman, B., who was supposed to have a tumor in the motor region, but this was not found, faradic excitation having been employed to corroborate the correctness of the position of the opening with regard to the parts supposed to be involved.

The operation was performed February 9, 1898. A bipolar electrode was used. The first application was made in the postcentral gyre, two and three-fourths inches from the mesal line; no movements resulted. The second application was in the precentral gyre, one and nine-tenths inches from the mesal line; the left fingers were flexed and the hand was partly flexed. The third application was at a point in the precentral convolution, one and one-half inches from the mesal line; the proximal phalanges and the wrist were partly flexed. A fourth application, made over a convolution in front of the precentral convolution, presumably at the same level, produced the same movements as the previous excitation.

Dr. Keen expresses some doubt in his report as to which was the precentral and which the postcentral convolution, but we have given his notes as they were originally made by him.

After an incision into the brain substance, exploration was made for a tumor, and it was believed, owing to the resistance offered, that the growth was present, but it was too deep-seated to remove. The dura was now closed, some brain tissue being lost. The bone was not replaced.

Observation 9. The patient was a man, aged twenty-eight years, in whose case the diagnosis of epilepsy following fracture of the skull was made by Dr. Keen. As he had had only two epileptoid seizures, and these both began by twitching in the left foot and leg, the case was thought to be a favorable one for relief by operation. Dr. Keen performed the operation November 30, 1898.

The skull was chiselled with gouge and hammer over a depression on the right side of the head, two and three-eighths inches from a point one and one-tenth inches back of the

middle of the inioglabellar line, this opening being nearly one inch in diameter.

When the bipolar faradic electrode was applied at the anterior part of the opening at about its middle, contraction of the left hand occurred. When thrust upward toward the middle line under the skull a slight contraction took place in the left leg.

A small opening was made in the dura to discover whether there was any clot or other lesion. As none could be found, the opening was closed by a single stitch and the incision then closed without replacing the bone.

From the description of the points of application, these were probably just in front or along the line of the central fissure.

Observation 10. The patient in this case was a young man, aged twenty-one years, upon whom Dr. Keen operated January 20, 1903, for the relief of epilepsy.

As the spasms always began by a peculiar sensation in the left foot, which extended up the leg and body to the head, it was decided to expose the leg area for exploration. The opening was osteoplastic, of truncated shape. Its upper border was two-fifths of an inch to the right of the mesal line. The length of the superior scalp opening was three and nine-tenths inches. The two oblique incisions for the sides of the opening converged to a base of one and seven-twentieths inches. This base was placed somewhat obliquely in front of the first incision, so that in truncating the opening its posterior side followed approximately the direction of the central fissure.

The operation was planned to have the central fissure traverse the opening from above downward, so as to about bisect it.

The bipolar faradic electrode was applied to the brain at the upper margin of the wound, in what were believed to be the precentral and postcentral convolutions. The report states that the left arm was immediately thrown into spasm (presumably after the first application and also after the second). The opening not being high enough to expose the leg centre, the bone was gnawed away to the sagittal suture and the flap of the dura was extended almost up to the margin of the longitudinal sinus. Both the precentral and the postcentral convolutions were faradized at this level. No response was gotten from the postcentral, but immediately when the precentral was touched with the electrode the left leg was thrown into a general spasm, lasting about the same time as the spasm from the previous application, which was from one-third to one-half a minute. After exploring the leg centre to the depth of one and one-half inches without result, the wound was closed.

This case is of much importance as indicating, first, that the area for the lower extremity is close to the mesal line, and, secondly, that it is probably situated entirely in front of the central fissure. It also shows the great importance of using cortical faradization in order to be sure that the proper level of the motor area has been uncovered.

Position of the motor zone with regard to the central fissure.

In order to get some data of value with regard to the position of the motor area with relation to the central fissure, we have made an analysis of the results of faradic applications in 25 cases, these including, as nearly as we could determine, 138 applications. The cases made use of were, in the first place, those published for the first time in the present communication, 10 in all; the 15 previously published cases included cases recorded as follows: By Keen, 7; by Mills and Keen, 1; by Keen and Sinkler, 1; by Lloyd and Deaver, 1; by Mills and Hearn, 1; by Nancrede, 1; by Ransom, 1; by Steiglitz, 1; and by Parker and Gotch, 1.

In preparing these data the cases recorded by Lamacq from unpublished notes furnished by Keen were used, the original manuscript of these cases having been examined through the kindness of Dr. Keen.

The result of the analysis was as follows:

Number of cases	25
Number of applications	138
Responses in front of central fissure	62
Responses behind central fissure	20
Responses in uncertain position as to the central fissure	14
No response in front of central fissure	14
No response behind central fissure	28

It was sometimes difficult to determine the number of applications and the exact position at which the electrodes were applied. It is for this reason that the responses in fourteen instances are recorded as having been in uncertain position with reference to the central fissure. Most of the applications included under this statement were made close to or along the line of the central fissure. It would probably be as nearly fair as possible to regard half of them as having been in front and half behind, remembering that we include those applications made along the anterior slope of the fissure as in front and those along its posterior slope as behind. In some instances in the recorded cases the statements were such as that a series of applications were made behind the central fissure or in the postcentral convolution without any result. It is probable, therefore, that the whole number of applications made in the 25 cases was somewhat larger than is given, but the results of the tabulation and analysis can, we believe, be relied on as accurate in their teachings. It will be seen that the data are overwhelmingly in favor of the view that the motor region is in front of the central fissure.

We might cite here as having some historical interest in

connection with the question of the precentral position of the motor region from the paper on "Cerebral Localization in its Practical Relations," published by one of us, Dr. Mills, in 1888: "Keen estimated the portion of the convolution as containing the hand centre as about one and one-fourth inches long, and he places the centre for the wrist and fingers in the pre-Rolandic gyrus, its lower limit being at three-eighths of an inch above the temporal ridge, and its upper end where it fused with that of the elbow 32 mm. higher up. The shoulder he placed still higher, while the centre for the upper face was in the same convolution below. These results correspond closely with those of Horsley. These facts of experiments on man would seem to uphold the view that the motor zone, in man at least, is much more extensive in front of than behind the fissure of Rolando. These results of Keen were all produced by excitation of the cortex anterior to the fissure of Rolando, supposing of course his determination of that fissure to have been correct."

MAIN SUBDIVISIONS OF THE MOTOR ZONE.

Accepting the view that the motor area is situated in front of the central fissure, what are its extensions and its main subdivisions? We believe it is largely limited in man, as in the anthropoids, to the precentral convolution projecting to some extent forward in one position. This forward projection is so situated as to include contiguous portions of the posterior extremities of the second and third frontal gyres. The chief subdivisions of the motor region are, from below upward: 1. The face area. 2. The area for movements of the eyes and head (the prefrontal projection), the centre of which is about on a line with the junction of the areas for the face and the upper extremity. 3. The area for the upper extremity. 4. The area for the trunk. 5. The area for the leg. The area for the movements of the face, in which we include movements of the tongue, lips, larynx, angle of the mouth, jaws, and eyelids, is a comparatively large one, extending from below upward to or just above the genu of the central fissure. The area for the arm next above this is a little more extensive vertically; next above comes a narrow trunk area, and above this the leg area, or at least that portion of it which is on the lateral aspect of the hemisphere. So far as the results obtained by faradization of the human brain go, these four areas would appear to be exclusively confined to the precentral gyre. The best vertical separation of these areas would probably be brought about by regarding the precentral gyre as subdivided vertically, or at least along the central fissure, into fourths; three of these fourths from below upward are occupied by the face and arm areas, the latter being somewhat larger vertically than the former; in the upper fourth are, situated from below upward, the areas for the trunk and leg, the former occupying only a narrow strip. The area for movements of the eyes and head is, as has already been indicated, on a level with a lower strip of the arm area and an upper strip of the face area. The area for the upper extremity is undoubtedly the largest of the main subdivisions of the motor zone, but is not as much in excess of that for the face as has been sometimes represented in diagrammatic schemes. The lower extremity is only represented on the lateral surface of the hemicerebrum by a comparatively narrow strip of the precentral convolution, but it has a considerable representation on the mesal aspect. In the diagram (Fig. 1) these main subdivisions are represented as nearly as possible in accordance with the above description.

As our present consideration of the subject of cerebral localization is particularly in connection with the surgical procedure, we shall not discuss the question of the extent and subdivisions of the motor zone on the mesal aspect of the hemisphere, simply saying that the leg area and probably centres for the anus and vagina are present in the paracentral lobule in front of the line of the central fissure.

SUBDIVISIONS OF THE FACE AREA.

The face area is probably subdivided in the human cortex, as represented in the diagram (Fig 1). The centres for the tongue, lips, larynx, and platysma have not been indicated as the result by us of a study of human cortical faradization, but have been adopted tentatively from other observations. All the other centres indicated, namely, those for the angle of the mouth, the eyelids, and the jaw, have been located from a study of the observation analyzed in this article. A centre for movements of the angle of the mouth has been several times determined in about the position shown in Fig. 1, namely, in the precentral convolution about the junction of the middle and upper thirds of the face area. Above this and perhaps a little forward is a centre for the eyelids. The centre for the alæ of the nose is probably near the same level, but has not been indicated in the diagram. The movements of the jaw would seem, from a study of the observations here recorded, to have a rather wide representation, but as nearly as could be determined primary movements of the jaw are elicited at a point above and somewhat behind the centre for the angle of the mouth.

With regard to the subdivisions of the face area given, a study of the new observations (1, 2, and 3) will show that these have been confirmed or indicated by them. The positions are also in accord with the previously recorded observations of Keen, Mills and Hearn, and others.

SUBDIVISIONS OF THE AREA FOR THE EYES AND HEAD.

The centre for movements of the head to one side is probably situated at about the position where the second, third, and precentral gyres come together, as indicated in

the scheme. A centre for conjoint movements of the head and eyes is probably situated just anterior to this position, and one for movements of the eyes alone still more forward. Objection has been made to giving distinct centres of representation for movements of the head and of the eyes. It seems to us quite clear, however, that such separate centres should be recognized. The simplest experiment shows that one can move the head to the left or to the right without moving the eyes, that the head and eyes may be moved together, or that movements of the eyes in different directions may be made independently of those of the head. Each separable voluntary movement has separate cortical representation. Forward movements of the head were produced in the case recorded as Observation 1 by excitation of a point about two and one-half inches from the mesal line, at about the position where the centre for head movements is indicated.

An interesting practical matter in connection with the question of a centre for movements of the head and eyes is that which is brought up by the fact that several observers have noted, as the result of human cortical faradization, that movements of the head sometimes take place toward the side on which the application is made. We recently had under observation a case of Jacksonian epilepsy in which the spasm began in the upper extremity of one side, the head turning during the convulsive attack toward the other side. We have observed other such cases, but have also had cases in which movements of the head and eyes were toward the side on which the spasm in the face or extremity occurred. The problem involved in these apparently contradictory observations as to the movements of the head and eyes is one which should receive further careful consideration.

SUBDIVISIONS OF THE ARM AREA.

The centres for movements of special parts of the upper extremities are situated in the precentral convolution, and counting from below upward are those for the thumb, fingers, wrist, elbow, and shoulder. The centre for the thumb movements is one which has received much attention in cortical faradization of the human brain, as from Horsley, Keen, Nancrede, Buchanan and Diller, and Parker and Gotch. The weight of the evidence is in favor of its being located in the most inferior portion of the arm area, close to and probably extending into the anterior slope of the central fissure. It has been placed by some observers in the postcentral convolution, but close reading of the reports of observations which indicate this position shows that the centre stimulated was either within the central fissure or so close to it that the stimulation of the posterior lip of the fissure may have been transmitted to its anterior slope.

FIG. 1.—Scheme of the motor zone and its subdivisions.

The centres for the movements of the fingers are situated just above the thumb area, and, for the most part, somewhat anterior to the latter. To a considerable extent the representation of different movements of the fingers has been determined. The index-finger movements are usually differentiated. Horsley obtained isolated flexion of this finger, its centre being in the precentral gyre, just above the thumb centre. One movement isolated by Keen was that of extension of the index finger, flexion of the other fingers, and rotation of the hand, this being the exact movement often made in pointing forward and from one side to the other. Extension of the index, middle, and little finger was also produced by Keen from a centre in the precentral convolution. Some of his observations would seem to show that each finger has

its separate centre. Mills and Hearn were successful in separating the centres for extension and flexion of the fingers. They found them above the centre for the angle of the mouth, the centre for flexion being behind and a little above that for extension. Keen obtained flexion of the fingers and of the wrist in the precentral gyre, near its anterior border. Ransom separated extension and flexion of the fingers by 12 mm. Horsley found the centre for the fingers in the precentral gyre, between the centres for movements of the index fingers and those for elbow movements. Bechterew found the finger centre between those for movements of the shoulder and

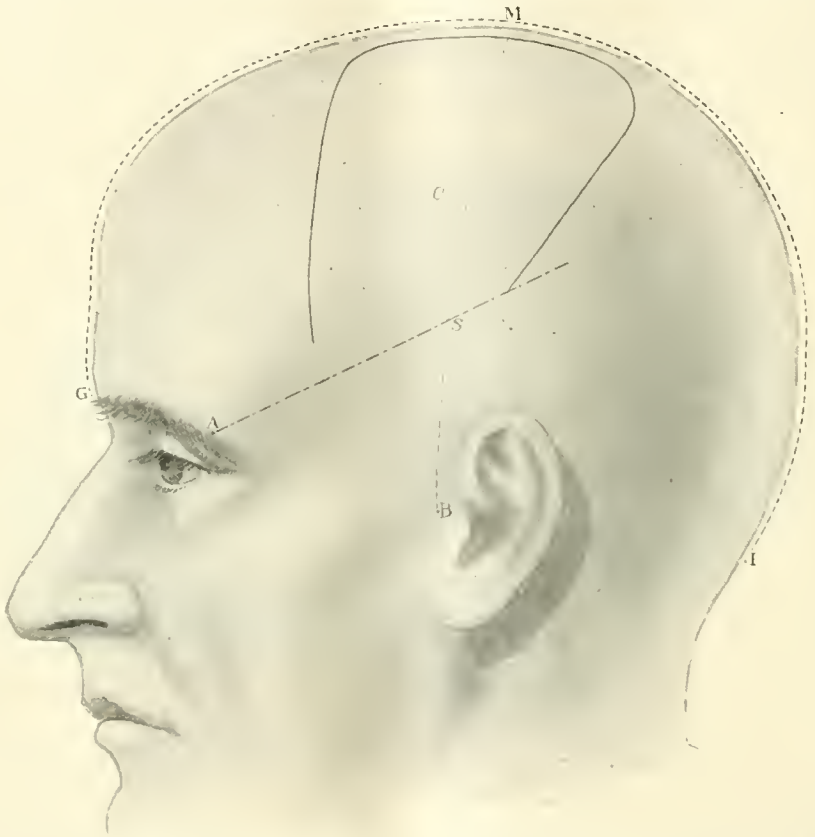

Fig. 2.—The Anderson-Makins lines and the usual osteoplastic flap for exposing the motor region: *G*, glabella; *I*, inion; *M*, midsagittal point, midway between *G* and *I*; *A*, external angular point; *S*, squamosal point, intersection of oblique and frontal lines at junction of middle and lower thirds; *B*, preauricular point; *C*, central fissure. Flap designed to be two-thirds anterior and one-third posterior to the central fissure.

thumb. Even lateral movements of the fingers have been isolated by human cortical faradization.

Movements of the wrist have been somewhat frequently observed in the human subject as the result of cortical faradization, usually however in connection with the movements of the finger or of the elbow. Horsley made a unique observation in one case, that of extension of the wrist with flexion of the fingers. The centre is located between the centres for the fingers and that for the elbow. In the case of Mills and Hearn there was first extension of the wrist and fingers, and at a point more posterior flexion of the same.

In several instances simple elbow movements have been produced by excitation of that portion of the precentral convolution which is situated just above the level of the representation of movements of the fingers. In one or two cases the same responses have been elicited by excitation apparently applied directly in the central fissure, and in one or two others when the application was behind or close to the fissure.

Elevation and other shoulder movements would appear to be represented in the most superior portion of the arm area, although it is difficult by cortical stimulation to get isolated movements of this portion of the upper extremity. In one or two instances the writers found movements of the shoulder elicited from a considerable portion of the arm area, and with a strong current, even from the postcentral gyre.

AREA FOR TRUNK MOVEMENTS.

We have not had any personal experience with regard to the situation of the centres for movements of the trunk, nor, so far as we know, have any such observations on the human subject been put on record. The experiments of Grünbaum and Sherrington indicate that the representation of trunk movements in the anthropoids is in a narrow strip just above the arm area, and therefore between it and the leg area, a

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localization in opposition to that of Horsley, who placed the centres for trunk movements on the lateral and mesal edges of the hemisphere in front of the leg area. M. Allen Starr, in one case of cortical faradization during an operation, observed movements of the trunk as the result of excitation of a centre just above the level of the arm area; this observation is corroborative of the results obtained by Grünbaum and Sherrington.[1]

SUBDIVISIONS OF THE LEG AREA.

The centres for movements of different segments of the lower limb have not been isolated as well as those for separate movements of the upper limb and of the face. Lamacq observes correctly that the movements of the lower extremity are little differentiated, and that the area for these movements is quite small, a view which has been confirmed by the experiments of Grünbaum and Sherrington, and recently by our own observations. On the lateral surface of the hemicerebrum the leg area in the human subject probably does not extend more than one-half or three-fourths of an inch from the longitudinal fissure. Movements of special parts of the upper extremity have additional and probably larger representation on the mesal aspect of the hemisphere. For the present we have adopted the order of representation of separate movements of the lower extremity as they have been long held, namely, counting from below upward, those for the hip, knee, ankle, and toes. A portion of this representation is on the mesal surface of the hemisphere.

THE TECHNIQUE OF CORTICAL FARADIZATION.

Certain difficulties in determining precisely what portion of the cortex is exposed to view are often realized by the surgeon and neurologist. This is especially true when but a limited area of the cortex is exposed and the pia mater is still intact. It seemed desirable that some plan should be adopted whereby the observations on faradic excitation of the cortex could be made and recorded with such accuracy that the results would be accepted as a contribution to our knowledge of the physiology of the motor cortex. The plan which we have recently adopted consists essentially in applying the electrode at certain fixed distances from the superior and posterior margins of the opening. Several studies were made upon the cadaver.

In outlining the flap for the exposure of the motor area, we have localized the Sylvian and central fissures by the Anderson-Makins method shown in Fig. 2. The flap is usually so mapped out as to have two-thirds of it in front and one-third behind the central fissure. Its posterior margin is made parallel and one inch behind the central fissure, and the superior margin one-half inch from the mesal line. The base of the flap is usually nearly on a level with the Sylvian fissure. If the flap as outlined on the skull commonly measures two inches at its base and four inches along the superior margin and sides, the opening in the bone is usually one-quarter to one-half inch narrower. A flap of about these dimensions is made in all cases in which the symptoms are strictly referable to the motor region.

In faradizing the cortex the electrode, according to a previously arranged scheme, is applied first to six different points, or to any of these; three of these should be about one-half or three-fourths of an inch in front of the posterior margin of the flap, presumably behind the central fissure; and three at one and one-fourth to one and one-half inches in front of the posterior margin, at levels corresponding to the selected points of postcentral excitation (Fig. 3 at points 1, 2, 3, 4, 5, and 6). Subsequent applications can, if desirable, be made to points intermediate and slightly anterior to and between the points first selected, as at *A*, *B*, *C*, and *D*. If the position of the centre for movements of the head and eyes should be in question, the exploration should always be made well forward in or near the position 7. Of course other points than those here given can be used at the judgment of the operator and according to the exigencies of the case. These should be designated in the description of the procedure according to their distance from the superior and posterior margins of the opening in the bone. As the superior border of the opening is at a fixed distance from the mesal line, by indicating the distance of the points of excitation from the superior margins, the distance from the mesal line is also at once obtainable. It will be seen that we do not depend at all upon any attempt to recognize by the sense of sight the fissures and convolutions.

In order to assure ourselves of the correctness of the positions of the points of excitation usually selected by us with reference to the central fissure, an osteoplastic operation was made on the cadaver after the plan employed in operation on the living. Our standard motor flap, bony and dural, was reflected and pins were first inserted into the brain around the margin of the opening, and also others at points presumably corresponding to those usually first selected by us for faradic applications; in other words, at the spots indicated at 1, 2, 3, 4, 5, and 6 in the illustration (Fig. 3). The calvarium was then removed, as well as the pia, and the positions of the electrodes relative to the Rolandic fissure definitely determined. The illustration (Fig. 4), which is made from a photograph of the cadaver operation, shows that the points of excitation usually employed by us are sufficiently accurate as regards their relations to the central

[1] Starr referred to this observation, which has not before been put on record, in the discussion of this paper at the meeting of the American Neurological Association in June, 1905.

fissure. In Fig. 5 these points are represented diagrammatically on the exposed brain surface.

If observations upon the effect of faradization of the cortex are to be of any immediate value to the observer or of any subsequent value as a contribution to our knowledge of the distribution of the motor centres, they should be made with as much care and accuracy as one would employ in the performance of any delicate physiological investigation. In the first place, in order that no time be wasted, the whole matter should be prearranged. In our observations, for example, a scheme as above outlined is employed. Each point to be faradized is given a number or a letter; a blank form is pro-

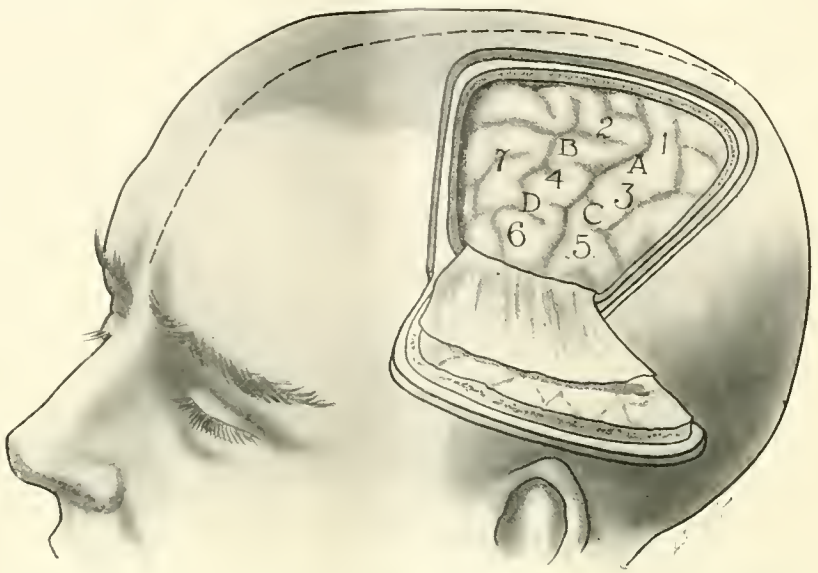

Fig. 3. Bony and dural flaps reflected so as to show the convolutions of the motor area. The numbers 1, 2, 3, 4, 5, 6, and 7, and the letters *A*, *B*, *C*, and *D* indicate the points of selection for cortical faradization.

Fig. 4.—Reflected osteoplastic flap in cadaver operation showing the places of insertion of pins at points of selection for precentral and postcentral faradization

vided containing these, so that at the operation the surgeon in dictating to the recorder the results of faradization does this with a number or letter which corresponds to a definite position with regard to the superior and posterior margins of the opening.

If these points are decided upon before the operation, a series of observations can be made in less than five minutes, and usually in half this time.

It is important, furthermore, to observe certain details in other particulars. One, for example, should test carefully the strength of the current before each application; one should begin always with a weak current, preferably rapidly interrupted. He should apply the current first to point No. 1 behind the central fissure, then without increase to point No. 2 in front of the fissure; if now at this second application no response occurs, the current should be carefully increased before applying it to points Nos. 3 and 4. If no response is obtained, it should then be again increased and applied to points Nos. 5 and 6. As soon as a response in movement is obtained this strength of current should be used as a standard for the succeeding applications.

If too strong a current is employed it may be so diffused as to stimulate centres situated some distance from the point at which the electrode is applied. If too strong a current is applied to the postcentral fissure, the response may be due to diffusion of the current to the precentral region. If the observations of Grünbaum and Sherrington upon the ape are correct for man, a weaker current might give no response in the postcentral and a positive response in the precentral convolution.

The question of the diffusion of the electric current is one of great importance in deciding the situation of separate or isolated centres. It is well known to electricians that a galvanic or faradic current applied to one nerve distribution, as for instance that to the extensors of the forearm, in a case in which the muscles supplied by this nerve are paralyzed, will fail, owing to conditions of disease, to cause response in the muscles being investigated, whereas, the current diffused to the nerve supplying the flexors gives a very decided response; in other words, it is simply the question of extrapolar diffusion of currents more or less strong.

It was apparently evident that in some of the cases in which response was produced by applications behind the central fissure, as for instance Observation 5, this was the result of diffusion of the current.

A study of the records of the older cases of bipolar faradization which have been collected by Lamacq and the writers shows with but little doubt that in many of these cases the current was of such strength as to make it impossible to decide from its use the question of the precentral or postcentral position of the motor region.

It is important that the electrode should be applied always first behind the fissure before attempting to stimulate the region in front of it. If this order should be reversed and the precentral convolutions stimulated first with a current sufficiently strong to excite a response, and the postcentral afterward, it is quite possible that, though using a current of the same strength, one might get a response from the postcentral convolution, when no response would have been obtained had the electrode been applied first to this convolution. This we have noted in our own cases and have attributed it to the fact that a centre once stimulated to the point

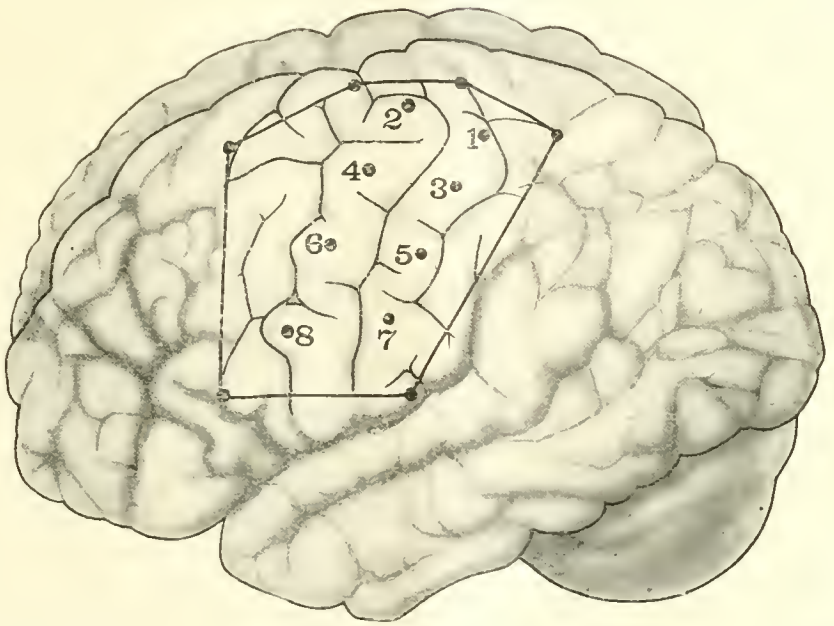

FIG. 5.—Drawing of the brain after calvarium and membranes were removed, showing the position of osteoplastic opening with reference to the fissures and gyres of the motor region. The numbers 1, 2, 3, 4, 5, 6, 7, and 8 indicate the preferable points for faradization of the cortex during the operation.

of reaction becomes so much more sensitive that it is affected by stimulation in regions adjacent to it.

Attention has been called recently by Sherrington, and Krause particularly, to the advantages of the unipolar over the bipolar method of faradization. With regard to this question of unipolar and bipolar faradization, it is of course well known that the earlier experiments in this country were nearly all bipolar, making use of Keen's bipolar electrode. These observations in some instances gave very satisfactory results. At the same time, on general principles, in the isolation of centres the unipolar application, if made under certain strict regulations, should give the more accurate results. Grünbaum and Sherrington and Krause used these unipolar applications in their well-known experiments on the brains of the anthropoids, the chimpanzee, orang-outang, gorilla, etc. In order that the best results can be obtained from unipolar faradization of the cortex, several matters should be kept clearly in view. In the first place, the electrode should be small. In our investigations a unipolar electrode, designed by one of us, Dr. Frazier, was used. This has been modified as the result of experience. In order that the pia and brain substance should not be punctured, the electrode should not be sharp. It should not be larger than the head of a pin. The instrument should be so handled that none of its conducting parts should come in contact with the dura.

The indifferent electrode should be at least four to six inches square. It should always be applied very carefully, so that all parts of it remain in contact with the skin during the entire application. It should be kept thoroughly saturated during the application with warm water or a hot salt solution. It should be placed carefully on one side of the mesal line, and preferably on the side of the operation. Perhaps as convenient position as any with regard to the surgical procedures and etherization is on the buttock or thigh of the same side. It may be held by the weight of the patient, but, owing to the possible changes in position of the patient, it is preferable that an assistant should be directed to keep it in place.

If these precautions are observed and the rules which have been given above with regard to the method of successive applications to get a standard current are employed, we believe that it will be found that the unipolar will have advantages over the bipolar method. If carried out systematically and expeditiously, the applications are absolutely harmless and in no way detrimental to the interests of the patient.

Craniometric Lines and Craniocerebral Relations.

Reference has been made to the shape and size of the opening used for the exposure of the motor area. In outlining this flap, one must first determine the topical relations between the Rolandic and Sylvian fissures and the skull cap. For this purpose, one or the other of the methods of craniocerebral topography may be used. According to the age of the patient and to the sex and race, there may be some variation in the relation of the cerebral convolutions to the calvarium; so that no individual method has been found which is invariably accurate. In our experience, as already stated, the Anderson-Makins lines have given satisfaction. Of the relative merits of these lines with those of Krönlein, we are not prepared to speak, since with the latter we have had as yet no experience. Krönlein's topographical lines are constructed on the same fundamental principles as those of Anderson-Makins, in that the rules for their application eliminate "absolute values and replace them with relative values, which are in proportion to the size of the skull and of the brain, and which vary accordingly in the individual case."

The Krönlein craniometer, a mechanical device constructed for the purpose of facilitating the application of the Krönlein method, has been spoken of so highly by those who have had experience with it that Dr. Frazier is importing one for his own use and he hopes to have an early opportunity to test its accuracy.

Horsley, Keen, and other surgeons, especially in this country and in Great Britain, have used chiefly the methods of Thane and Hare, with the cyrtometer of Wilson, or the fissure meter of Horsley, in fixing the position of the central fissure, and therefore of the motor region. While the results with these methods seem, from the recorded cases, to have been accurate, we have not resorted to them because the Anderson-Makins method, with its modification, has proved satisfactory in the cases in which we have applied it.

Having established and marked upon the scalp lines corresponding to the central fissure and Sylvian fissure, we map out the flap for exposure of the motor cortex, so that at least two-thirds of the opening will lie in front and only one-third posterior to the Rolandic fissure, the flap extending from the Sylvian fissure to within one-half inch of the median line. In addition to this, prior to the operation, a forward central extension of the opening should be outlined on the scalp to cover what is believed to be the most anterior portion of the area for the eyes and head. If the centres for the eyes and head are found not to be completely exposed, the overlying bone can be removed in this forward direction, as outlined, with the rongeur. The usual flap of three and one-half or four inches will, in most cases, however, be sufficient to uncover all that is necessary of the region for movements of the eyes and head. If the opening in the skull, which is outlined with the view of making its superior border one-half inch from the mesal line, is found not to uncover the centres for the trunk and upper extremity, the rongeur forceps can be used to extend the opening to the longitudinal fissure,

care being taken, of course, with regard to the longitudinal sinus.

In looking over the results of our earlier operations, we found that when the flap was equally divided by the central fissure it was necessary occasionally to enlarge the opening forward, in order to fully expose the lesion. Since the more recent plan of making the opening two-thirds in front and one-third behind the fissure has been adopted, it has never been necessary to enlarge the opening backward. The clinical data, taken together with such evidence as we have accumulated from faradization of the cortex, lead us to believe that not only have we been justified in advancing the position of the flap so far forward, but that in the future, in all probability, it will be unnecessary to uncover even one-third of the cortex behind the central fissure for the exposure of motor cortical lesions. Probably a relation of three-fourths to one-fourth will be found to be a suitable proportion.

Presuming, as we believe, that the motor region is entirely or almost entirely precentral, one-third or one-fourth of the osteoplastic opening should be posterior not only for purposes of freer exploration, but also because of the fact that the central fissure at about the junction of its middle and lower thirds bends backward slightly, constituting the genu of the fissure. Unless one-third or one-fourth of the opening is designed to be behind the fissure, the posterior margin of the flap might encroach upon the lower third of the fissure

THE OCCASIONAL CLINICAL RESEMBLANCE BETWEEN CARIES OF THE VERTEBRÆ AND LUMBOTHORACIC SYRINGOMYELIA, AND THE LOCATION WITHIN THE SPINAL CORD OF THE FIBRES FOR THE SENSATIONS OF PAIN AND TEMPERATURE.[1]

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(From the Neuropathological Laboratory of the University of Pennsylvania and the Philadelphia General Hospital.)

Tuberculous caries of the vertebræ (Pott's disease) is so common that one might think there is little new to say about it, and yet the resemblance it may present to the lumbothoracic form of syringomyelia has not received much attention. There is no doubt that the resemblance between these two diseases in their clinical manifestations at times may be so great that a correct diagnosis may be very difficult. A case of caries of the vertebræ recently under my care presented the symptoms of lumbothoracic syringomyelia in so striking a manner as to make a diagnosis uncertain.

Cases of syringomyelia are numerous in the literature and much has been written about the disease since Schultze and Kahler first recognized the symptoms in 1882 (Mertens). Minor mentions that Schultze, and Kahler and Pick first in 1883 confirmed the clinical diagnosis by necropsy. Usually the cavity is in the cervicothoracic region, although not necessarily confined to this part. It may, however, be limited to the lower thoracic and lumbar regions. Such cases are of rare occurrence. I believe, however, I have seen two or three clinical examples of this type of syringomyelia.

Schlesinger, in his wonderfully thorough work on syringomyelia, remarks that the lumbothoracic type is relatively rare as compared with the cervical type, but its existence has been established by necropsies. Cavities in the lower part of the cord frequently are small and cause no symptoms, but in other cases there may be severe pain and paræsthesia of heat and cold sensations as early symptoms. The spinal column may show kyphoscoliosis early, and may be tender to pressure. Weakness of the lower limbs soon develops, even within a few hours, and may be associated with involuntary jerking movements. Intense atrophy may follow. The lower limbs are usually spastic and the tendon reflexes exaggerated. The symptoms may be confined to one limb a long time, or may develop rapidly in both lower limbs. Girdle sensation is not uncommon. Dissociation of sensation is present, although tactile sensation may be much involved. Ataxia may occur. Vesical and rectal implication are not rare, and may be transitory; the sexual functions also may be affected. Trophic disturbances (mal perforant, cutaneous gangrene, œdema) may be seen in the lower limbs.

As examples of the lumbothoracic type with necropsy, Schlesinger refers to the cases of Lenhossék, Vulpian, Hitzig, Kahler and Pick, and a doubtful case of Oppenheim. He refers to the clinical cases of Lutzenberger and de la Camp. As an example of tumor with cavity within the spinal cord in the lumbar region, the case of Simon (Case VIII.) is mentioned. Clinical cases are referred to as reported by Brunzlow, Oppenheim (2), Mills, Rummo (2), and Tornow.

As examples of clinical cases of the lumbosacral type of syringomyelia (there seem to be none with necropsy) Schles-

[1] Read by invitation before the Section on Neurology and Psychiatry of the Medical and Chirurgical Faculty of Maryland, March 8, 1905.

inger[1] refers to the cases of Oppenheim, Graf, Dercum, Köbner, Gnesda, Minor, Manner, Mertens, and three cases of his own, but in one of his three cases (Case LII.) the upper limbs also were implicated.

It is hard to understand how the diagnosis of syringomyelia could have been made in Lenhossék's case, as given in abstract by Schlesinger, because no dissociation of sensation and no trophic lesions are mentioned. The symptoms were suggestive of meningomyelitis, and the patient had been guilty of excesses, and syphilis might have been suspected. There seems to have been nothing clinically characteristic in Vulpian's case, and the pathological findings, as given by Schlesinger, are like those of meningomyelitis. Hitzig's case could not have been diagnosed during the life of the patient. Kahler and Pick's case or Simon's could hardly have been diagnosed as one of syringomyelia from the symptoms; therefore, there seems to have been no case of syringomyelia in the lower part of the cord with necropsy in which the diagnosis could have been made in life.

Some of the clinical cases mentioned by Schlesinger can hardly be regarded as examples of syringomyelia confined to the lower part of the spinal cord.

In the case reported by de la Camp,[2] trophoneuroses and sensory disturbances of the syringomyelic type in the lower limbs, exaggeration of the patellar reflexes, gradual convexity of the vertebral column without a distinct prominence (gibbus), led to the diagnosis of syringomyelia, but there was no necropsy.

The report of O. Brunzlow's[3] case (Case IV.) is far from convincing, so far as the existence of lumbothoracic syringomyelia is concerned. No necropsy was obtained. The symptoms developed after trauma.

The cases reported by McConnell from Dr. Mills'[4] service were interesting, as they were among the earlier cases of syringomyelia reported in America, but they were not of the lumbothoracic type.

E. Tornow's[5] case can hardly be accepted as one of uncomplicated lumbothoracic syringomyelia.

Graf's[6] patient (Case III.) had arthropathies of the left knee and foot, exaggeration of the patellar reflexes, and syringomyelic dissociation of sensation in the lower limbs. The case was regarded as one of syringomyelia, and the diagnosis seems to have been correct, although no necropsy was obtained.

Dercum's[1] case probably was one of syringomyelia of the lower type.

Neither of the two cases reported by Köbner[2] seems to have been an example of lumbosacral syringomyelia, and in each case syphilitic infection had occurred. I should be inclined to regard the pathological process in these cases as syphilitic meningomyelitis.

Max Gnesda's[3] case is surely a doubtful one of lumbosacral syringomyelia.

Minor's[4] case, if I have found the right report, was with necropsy, but was complicated by spina bifida, meningocele, and hydrocephalus.

Simon's[5] case (Case VIII.) was with necropsy and was one of lumbar syringomyelia.

Merten's[6] patient probably had had syphilis, and had paræsthesia of the hands and of the occipital region and of the mucous membrane of the mouth; he had also diabetes. The lower limbs were weak and presented the syringomyelic dissociation of sensation. The vertebral column was not affected. The patellar reflex was normal on one side and diminished on the other. Trophic disturbances were present in the feet. Mertens believed the case was one of syringomyelia of the lower part of the spinal cord, but there was no necropsy, and the case was a complicated one.

Thus, without examining all the reported cases, we find that the examples of syringomyelia of the lower type are not numerous. I report the following as a case which should be placed under this heading:

Joanna M., an Italian woman, aged thirty-four years, was admitted to the Philadelphia General Hospital May 11, 1903. The notes I dictated June 3, 1903, are as follows:

A history was obtained, but is unreliable, as the woman replies in the affirmative to almost every question put to her. She is said to have had subjective pain in both lower limbs about four months, but none in the upper limbs. The pain was said to have been first in the right lower limb and developed before the weakness. It is impossible to determine how real this pain was. She had one child seven or eight years ago, and it died two days after birth.

She has less perception of pain in the right lower limb, both thigh and leg, than in the left, as shown by the fact that she does not withdraw the right lower limb from irritation as promptly as she does the left. The right lower limb is not spastic, and, indeed, seems flaccid. The left lower limb is decidedly spastic. There is no patellar reflex on the right

[1] Die Syringomyelie, Hermann Schlesinger, second edition, 1902. Franz Deuticke, Leipzig und Wien.
[2] Berliner klin. Wochenschrift, March 4, 1901.
[3] Inaugural Dissertation, Berlin, 1890.
[4] Journal of Nervous and Mental Disease, 1894.
[5] Inaugural Dissertation, Berlin, 1893.
[6] Beiträge zur klinischen Chirurgie, 1893, vol. x. p. 517.

[1] Journal of Nervous and Mental Disease, 1898, p. 488.
[2] Deutsches Archiv für klinische Medicin, vol. xix. p. 169.
[3] Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, 1899, vol. iv. p. 744.
[4] Zeitschrift für klinische Medicin, 1898, vol. xxxiv. p. 373.
[5] Archiv für Psychiatrie, 1875, vol. v. p. 156.
[6] Beiträge zur klinischen Chirurgie, 1901, vol. xxx. p. 121.

side, not even contraction of the quadriceps muscle from tapping the patellar tendon. The Achilles reflex is absent on the right side. The Babinski reflex is present on the right side, but the movement of the big toe is not very marked. The Achilles jerk is exaggerated on the left side. Ankle clonus is not obtained at present examination (it was obtained on the left side five days later).

Babinski's reflex on the left side is very distinct. Both lower limbs are weak, but the left is much weaker than the right. If well supported the woman can take some steps, and in doing so moves the right lower limb forward and drags the left lower limb. She always steps out with the right lower limb.

The upper limbs and face do not appear to be involved. Pressure over the back, she says, is painful in the lower thoracic and lumbar regions, but deep pressure causes no change of expression.

Further notes were made by me December 12, 1903:

The right lower limb is flaccid. The right patellar reflex is completely lost, even on reinforcement. The left patellar reflex is much exaggerated. The left lower limb is spastic, but probably not so much so as at the former examination. Patellar clonus is not obtained on the left side. Ankle clonus on the left side is persistent. No indication of clonus is seen on the right side. Achilles jerk is very feeble on the right side, and it is doubtful whether it is present. Pain sensation is distinctly present in the lower limbs.

February 23, 1905. There are no deformities of the vertebral column, and no trophic disturbances of the lower limbs. Voluntary power in the right lower limb, both in thigh and leg, is about normal. Voluntary power in the left lower limb, both in thigh and leg, is distinctly diminished, but not lost. The lower limbs are not distinctly atrophied.

The patellar reflex is greatly exaggerated on the left side, and there is distinct patellar clonus. Ankle clonus is persistent on the left side. Babinski's reflex is typical on the left side. The patellar reflex is completely lost on the right side, as is also the Achilles jerk on this side. Babinski's reflex is also distinct on the right side, but not quite so pronounced as on the left side. Light touch is perceived promptly in both lower limbs. Pin-prick is perceived in the right lower limb if the prick be deep, but there is undoubtedly diminished pain sensation in the right lower limb. Sensation for heat is much diminished in the whole right lower limb, and probably over the right lower part of the abdomen, although it is uncertain whether there is diminution to heat sensation over the lower part of the abdomen. Sensation for heat is very prompt in the entire left lower limb. Cold sensation is probably diminished in the entire right lower limb. In walking the left lower limb is spastic, and the woman swings it a little from the hip and scrapes the toes of the left foot along the ground very markedly. The right lower limb is thrown unnecessarily far forward in walking, and the heel is brought down first. The left lower limb is a little spastic in passive movements, but the right lower limb is flaccid.

Biceps and triceps tendon reflexes are prompt in the upper limbs, but it is difficult to say whether they are exaggerated. The thenar and hypothenar eminences are well developed in each hand.

The right pupil is a little larger than the left, but the reaction to light is prompt. Sensation for pain seems normal on each side of the face.

A brief summary of this case is as follows:

The condition in this patient has remained unchanged during almost two years. As she cannot understand English and is not very intelligent, I am unable to obtain any account of the development of the disease, even by an interpreter. The symptoms are confined to the lower limbs, if we exclude the inequality of the pupils, and are as follows: In the right lower limb pain and temperature sensations are much diminished; while tactile sensation is prompt, the patellar tendon reflex and Achilles tendon reflex are lost; the limb is flaccid, and its movements in walking seem to be a little ataxic, while voluntary power is about normal. In the left lower limb all forms of sensation are normal, weakness is distinct, the patellar reflex is exaggerated, and patellar clonus and ankle clonus are present; the limb is a little spastic, and its toes are dragged a little when the patient walks. Babinski's reflex is present on each side. It is a Brown-Séquard paralysis (weakness in the left lower limb, dissociation of sensation in the right lower limb), with spasticity and exaggerated tendon reflexes in the left lower limb, and flaccidity and loss of tendon reflexes in the right lower limb.

A lesion in the left half of the spinal cord in the thoracic region and above the lumbar region would explain the weakness of the left lower limb and the exaggeration of the tendon reflexes and the presence of the Babinski reflex in the left lower limb; also the dissociation of sensation (preservation of tactile sensation, with much impairment of temperature and pain sensations) in the right lower limb, because the sensory fibres from the right lower limb cross soon after entering the cord to the left side. We must assume that the crossed pyramidal tract and other parts of the lateral column, especially Gowers' tract on the left side, are affected, but the gray matter of the anterior and posterior horns of this side cannot be diseased in the lumbar region, or there would be atrophy and loss of tendon reflexes in the left lower limb. To explain the loss of tendon reflexes and the flaccidity in the right lower limb without atrophy, we must assume that there is a lesion of the right posterior horn of the lumbar region without involvement of the right anterior horn, as no atrophy has occurred, even after two years, and we should expect atrophy were the anterior horn cells diseased. The lesion may affect

slightly the right crossed pyramidal tract, because of the Babinski reflex and possibly slight weakness on the right side, but it cannot greatly impair this tract, as the weakness of the right lower limb is comparatively slight; nor can it involve much of the right lateral column, as sensations of pain and temperature are normal in the left lower limb. The lesion must, therefore, involve much of the left half of the cord in the thoracic region, but not extend into the left lumbar region very far, and must implicate the right posterior horn in the lumbar region; it must also be a slowly developing lesion, and nothing suits these conditions so well as syringomyelia. In the case of syringomyelia reported by Dr. Dercum and myself, the cavity in the cervical region was strictly confined to one posterior horn, although below the cervical region it implicated a large part of the transverse area of the cord.

Cases with symptoms of syringomyelia from fracture I do not consider here, as the history of injury and the signs of fracture make a mistaken diagnosis improbable. Hemorrhage into the cord, occurring as a result of fracture, as shown by Minor, may cause the dissociation of sensation of the syringomyelic type, but this disturbance of sensation may also be caused by myelitis, and in 1903 I[1] reported a case of traumatic myelitis with necropsy without central hemorrhage, in which the dissociation of sensation of the syringomyelic type was present (preservation of, or slight impairment of, tactile sensation, with marked implication of pain and temperature sensations). The lesions in the cervical region in that case were diffuse.

In my experience spontaneous pain or pain on pressure over the vertebræ is not a very common symptom of syringomyelia, although it does occur, and it is mentioned by a number of writers as a sign of the disease. The clinical picture of lumbothoracic syringomyelia we may expect is paralysis or paresis of the lower limbs, with the syringomyelic dissociation of sensation and possibly trophic disturbance in the lower limbs; kyphoscoliosis, especially low in the vertebral column; usually exaggeration of the tendon reflexes of the lower limbs, but sometimes loss of these reflexes, if the cavity involves the reflex arcs, and possibly involvement of bladder and rectum.

It is well to study the literature to see whether the syringomyelic symptom group occurs as a result of lesions other than syringomyelia. The dissociation of sensation of the syringomyelic type I have observed in the case of traumatic myelitis with necropsy referred to above, and also in a case of syphilitic meningomyelitis with necropsy, reported by Dr. C. K. Mills and myself.[2] In these cases the lesions were widespread in a transverse section from the cervical region. It is hard to understand the dissociation of sensation occurring in these cases, but we may conclude that fibres of tactile sensation are more widely distributed in the spinal cord or are more resistant than are the fibres of temperature and pain sensations. These cases do not afford proof for or against the view that fibres of temperature and pain sensations are contained in the tracts of Gowers.

Minor[1] has shown that a zone of the syringomyelic type of dissociation of sensation may be found just above the level of complete anæsthesia in cases of traumatic myelitis.

Van Gehuchten regards the syringomyelic dissociation of sensation in the lower limbs as exceedingly rare in cases of compression of the spinal cord, and he reports 2 cases of this type, although the diagnosis of the lesion is somewhat doubtful. He refers to a similar case reported by Bruns, to 4 cases reported by Vines, 1 being a case of Pott's disease, and to the case of Pott's disease reported by Edsall, and to the case of compression of the cord reported by Marinesco. In all these cases the syringomyelic disturbance of sensation was in parts of the body innervated below the spinal lesion, while in Minor's cases the dissociation was in the area innervated from the portion of the cord just above the area of compression.

In Marinesco's[2] case of compression of the cord the syringomyelic dissociation of sensation at first was in the lower limbs and in the anterior and posterior parts of the trunk. Later anæsthesia was found in the feet and legs.

Dissociation of sensation from pressure of a spinal tumor has been observed (Boettiger,[3] Cushing[4]).

Van Gehuchten[5] believes the dissociation of sensation is dependent upon a lesion of Gowers' tract, and that pain and temperature fibres are contained in this tract. This, he remarked, was a new idea, but if this view could be sustained it would make clear many problems of the pathology of the nervous system. He first expressed in 1893 the opinion that the tract of Gowers contains fibres of pain and temperature sensations. His views have been supported by Brissaud, Lloyd, Schlesinger, and others, but no one has offered any *proof* of the correctness of this opinion. Van Gehuchten has not had any cases with necropsy sustaining his opinion, and in Lloyd's case the lesion was too extensive to afford proof that the tract of Gowers alone contained the fibres of pain and temperature.

One of Van Gehuchten's arguments is that the tract of Gowers is the only long tract in the lateral column likely to transmit fibres of pain and temperature. This is a proper method of reasoning, but sensation possibly may be transmitted by relays of fibres, by connected systems of neurones

[1] University of Pennsylvania Medical Bulletin, Feb., 1903.
[2] Journal of Nervous and Mental Disease, January, 1903.

[1] Neurologisches Centralblatt, 1898, p. 537.
[2] Semaine médicale, 1898, p. 154.
[3] Archiv für Psychiatrie, vol. xxxv, p. 83.
[4] Annals of Surgery, June, 1904.
[5] Semaine médicale, 1899, p. 113, and Journal de neurologie, July 20, 1897, p. 262.

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in the anterolateral columns. Many have held that sensory fibres are probably contained in the anterior or lateral columns; therefore, when the lesion involves much of these columns, we have no proof that Gowers' tract alone conveys fibres of pain and temperature. Petrén,[1] Mai,[2] and Piltz,[3] of still more recent writers, express the opinion that fibres for the sensations of pain and temperature are contained within Gowers' tract.

The case of caries of the vertebræ presenting symptoms of lumbothoracic syringomyelia I have had the opportunity to study is as follows:

John R., colored, aged twenty-three years, was admitted to my service in the Philadelphia General Hospital August 31, 1904, and, after passing into Dr. Mills' service, came again under my care. He died January 13, 1905. Chief complaint August 31, 1904, pains in legs, abdomen, and back. Last January he fell from a ladder and injured his left hip slightly. He gives a history of gonorrhœa last summer, but denies specific disease.

He began four months ago to have dull pains in the lumbar region of the back and abdomen and on the left side. Then numbness in the feet developed and gradually extended up both legs. He has gotten weaker generally during the past two months. When he elevates his arms it causes pain in his back. He has not felt girdle sensation. At times he gets dizzy and staggers. Sight and hearing have not been affected. He is a fairly well-developed male. He has a number of scars on the abdomen, which he received in childhood as a result of of burns, which he says were not painful. The lungs appear to be normal.

I made the following notes September 1, 1904:

There is marked deformity of each knee which is not very great while he is sitting, but when he is standing he has extreme genu valgum, such as would occur from a relaxation of the ligaments. He has no pains in his limbs, but the lower limbs from the knees down feel as if asleep. The deformity of the lower limbs has existed only about five years. One brother and three sisters of the patient are living and have no deformity of the limbs. The man is not emaciated. The patellar reflexes are a little exaggerated on both sides. Resistance to passive movements in the lower limbs is slightly diminished. Sensation for touch in the lower limbs is normal or nearly normal. Sensation for pain is abolished or nearly abolished in the lower limbs. Sensations for heat and cold are almost lost in the lower limbs below the knees, much impaired in the thighs and lower part of the trunk, and are normal in the upper limbs.

Sometimes he cannot hold his urine, but has no difficulty in passing it. His bowels are not usually constipated. When standing his feet are far apart, because of the deformity of his knees. He sways very slightly with his eyes open, but sways distinctly when they are closed. The gait is difficult because of the bilateral genu valgum. The Achilles jerk is absent on each side. The Babinski reflex is not present on the left side, the movement of the toes not being positive in any direction. It seemed to be present on the right side two or three times, and then was exhausted. He is flat-footed on each side. No girdle sensation is felt. There is a very slight kyphosis in the lower thoracic region about the tenth thoracic vertebra with slight scoliosis.

The upper limbs are normal.

The pupils are equal; the irides contract promptly on both sides. The cranial nerves are not involved. Sensations in the face for touch, pain, and temperature are normal. Seventh, twelfth, and fifth nerves are normal, as are the extraocular muscles.

On September 16, 1904, he fell down-stairs backward, was unable to pick himself up, and was carried to bed, where he has remained. Immediately after the accident he was unable to stand or walk, and had considerable pain in the lumbar region.

Dr. McConnell made the following notes: October 2, 1904:

He is almost completely paraplegic; slight evidence of attempt to move the limbs is observed in contraction of the quadriceps. When the limbs are supported under the knees the patient can kick slightly. He is unable to dorsally flex either foot. Sensation to touch seems to be lost in the whole of the right leg, but is quite well preserved in the left leg, penis, and scrotum, and everywhere else in the body. Sensation to temperature is lost everywhere over the right leg and foot; also over the left foot, but preserved everywhere else. (It is not said that pain and temperature sensations were normal in other parts.) Sensation to pain seems to be lost and preserved in the same distributions as are the other sensations. The patellar reflex is very markedly increased on each side. Ankle clonus is obtained on each side. Babinski's sign is not positively obtained, although there seems to be an occasional abnormal response to plantar irritation on each side. Achilles jerk is lost on each side. Gastrocnemius and quadriceps jerks are both retained. Squeezing the testicles does not cause any pain. Cremaster reflex is questionable.

October 17th. He complains of pain on both sides of the abdomen and in the back. Percussion at the base of either side of thorax causes pain. There is a dull area on the right side, extending from the fifth rib to the costal margin. Left side is resonant.

27th. Sensation to touch seems to be everywhere present in the right limb, as well as in the left; even the soles of the feet seem to respond to touch stimulation. Pain sense is

[1] Cited by Mai.

[2] Archiv für Psychiatrie, 1904, vol. xxxviii. p. 182.

[3] Neurologisches Centralblatt, March 16, 1905.

irregularly present, the response to pain stimulation being very uncertain and not always correct, although for the most part he *seems* to have pain sensation. Temperature stimulation, while better responded to than formerly, is not always correctly responded to. He will speak of hot as cold and cold as hot within very small areas on the surface. He is unable to tell which of the toes is grasped on the right side, but at once responds when the left foot is examined in a similar manner.

He has developed three bedsores within the last few days.

November 30th. Temperature runs up at night, and he sweats rather profusely. He cannot move his legs at all and complains of pain in the right knee. Patellar and ankle clonus are obtained on both sides. Exaggerated knee-jerks and Babinski's reflex are present on both sides. Tactile sensation is dulled in the legs, and he has some paræsthesia.

December 10th. The man says he can hold his urine well, and has to percuss the abdomen in order to start the flow of urine. Bowels are constipated. He is completely paraplegic; cannot move even a toe. Knee-jerks are both markedly increased. Patellar clonus is marked on each side. Ankle clonus and Babinski's reflex are present on each side. Tactile sensation is preserved on the right side. He seems unable to appreciate the difference between heat and cold over both legs generally. He almost always responds correctly to the application of cold, but is unable to tell when heat is applied until a point is reached on the inner surface of both thighs corresponding to the riding breeches' area. The scrotum and penis are sensitive to heat and cold. On the posterior surface of both thighs the response to heat again corresponds in its lower border to the riding breeches' area. Above this lowest line sensation seems to be normal. The trunk and upper extremities seem to be normal in response to all forms of sensory stimulation. The legs are considerably wasted, particularly in the inner side of the thighs and the calf muscles of the right leg; here, however, the wasting is relative as compared with the left leg, both calves being quite small. No wasting is seen in the feet, but there is a very marked degree of desquamation, probably trophic, more on the left leg, especially the outer surface.

In January, 1905, the patient came again under my care.

January 8, 1905. He has been having increased temperature and is becoming more emaciated, but has no cough. There is great wasting of the thigh and calf muscles. He complains of pain in the legs, but no girdle sensation. Incontinence of feces is present, although he is generally constipated, but has good control over the bladder. Sensation over the legs is felt for strong pin-prick, but is impaired or lost for light touch; sensation in the right leg being sometimes referred to the left.

11th. He is much weaker and almost stuporous. Abdomen is tympanitic, and there is a nodular mass palpable in the left umbilical region, and the same less evident to the right slightly higher up. Twitching of arms and fibrillary tremors of face are observed. Incontinence of urine and feces have been present since yesterday.

12th. He is comatose and lies with his head inclined to the right and persistently refuses to turn it to the left. He has irregular feeble movements of both upper limbs and fibrillary twitching of facial muscles of both sides, especially of the right side. Head is held very stiffly to the right. Eyes are held also far to the right. The right upper limb is moved freely when stuck with a pin; the left upper limb is moved only slightly when it is stuck, and is paretic.

When the face is stuck with a pin contraction of facial muscles follows on each side. Pin-prick is certainly felt, both in the face and upper limbs. Passive movement of head to left causes much pain. Sticking either lower limb with a pin causes no movement. Plantar reflex is very much exaggerated on each side. Babinski's reflex is present, but somewhat indistinct on the right side, and uncertain on the left. The patellar reflex is present, but very weak on each side, not causing any movement of the leg, and is detected only by contraction of the quadriceps. It is impossible to determine whether the left leg is more paralyzed than the right, because when either leg is allowed to fall it drops lifeless. Some tendency to flexion contraction of each upper limb is seen at the elbow, especially on the left side.

The necropsy was made January 14, 1905, by Dr. John Funke, whose diagnosis is as follows:

Miliary tuberculosis of lungs, spleen, kidneys, liver, and of right pleura; fibroid myocarditis, spinal caries, large psoas abscess, external spinal pachymeningitis.

My microscopic study of the spinal cord shows a tubercle in the right lateral column at the extreme lower end of the thoracic cord and involving the area of Gowers' tract. About one-half to one inch higher another tubercle is found in the left Gowers' tract. These tubercles are small in all diameters. The cord does not show any compression from the external pachymeningitis.

Sections from the lumbar region show marked degeneration of each crossed pyramidal tract. The inflammation of the pia here, as everywhere, is very intense. There is also a round-cell infiltration about the vessels within the cord and within the nerve roots external to the cord. Marchi sections show distinct recent degeneration almost confined to the crossed pyramidal tracts. The nerve cells of the anterior horns stained by thionin appear to be normal.

Sections from the lower thoracic region show intense recent degeneration in the crossed pyramidal tracts, and also diffuse recent degeneration in other parts of the transverse section. Here and there in all the white columns are holes where nerve fibres have disappeared. Here also perivascular cellular infiltration within the cord is pronounced. The tubercles are degenerated at the centre and contain giant cells.

Sections from the upper thoracic and cervical regions stained by the Weigert hæmatoxylin method or acid fuchsin do not show distinctly secondary degeneration, but here, as everywhere in the cord, the pia is greatly invaded by round cells, and there is also some perivascular cellular infiltration within the cord.

Marchi sections from the cervical swelling show recent degeneration in the columns of Goll, the direct cerebellar tracts, and the tracts of Gowers. The remainder of the anterolateral columns seems to be almost entirely free from recent or old degeneration. The nerve cells of the anterior horns in the cervical region by the thionin stain seem to be normal.

The cellular infiltration of the pia over the medulla oblongata and about one of the optic nerves is as intense as over the spinal cord, and there is slight perivascular cellular infiltration within the medulla oblongata.

A brief summary of this case is as follows: A man, aged twenty-three years, began to have pain in the lumbar region and abdomen four months before he came under my observation. Numbness was soon felt in the feet, and gradually involved the lower limbs below the knees. When standing he had extreme genu valgum, which had existed about five years. He had scars on the abdomen, which he said were the result of painless burns in childhood. Resistance to passive movements was slightly diminished in the lower limbs. Sensation for touch was normal or nearly normal in the lower limbs, but sensation for pain was abolished or almost abolished in these parts. Temperature sensation was almost lost in the lower limbs below the knees, and much impaired in the thighs and lower part of the trunk. Walking was difficult because of the deformity of the knees. He had a slight kyphosis at about the tenth thoracic vertebra. The upper limbs and face were not affected.

After a fall backward down a flight of steps he became completely paralyzed in the lower limbs. Sensation for touch was then lost in the right lower limb for a time, but was preserved in the left lower limb. Sensations for temperature and pain were lost in the right leg and foot and in the left foot, but were preserved elsewhere, although it is not stated that they were normal elsewhere. The patellar reflexes were much exaggerated, and Babinski's sign was present.

Still later sensation for touch was found preserved everywhere in the lower limbs. Sensation for pain was irregularly present in the lower limbs, the response to pain stimulation being very uncertain, and sensation for temperature was also much impaired in the lower limbs.

Tuberculous meningitis and caries of the vertebræ were found, and a small tubercle was present in the right lateral column at the extreme lower end of the thoracic cord, involving the area of Gowers' tract. About one-half to one inch higher another small tubercle was found involving the left tract of Gowers. Although there was some myelitis, it was very evident from the symptoms that it had chiefly developed after the fall down the flight of steps, as at the time the patient first came under my observation weakness in the lower limbs was slight. He lived four months after the accident.

FIG. 1.—Small tubercle in the right lateral column, extending forward into Gowers' tract.

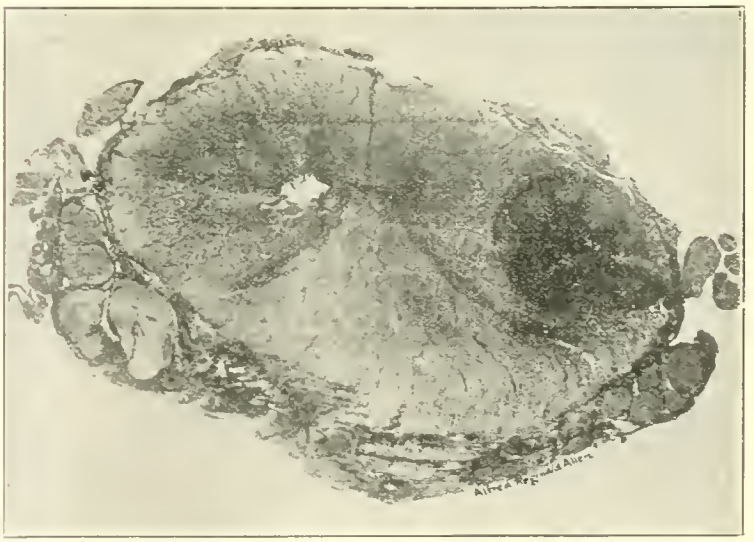

FIG. 2.—Small tubercle in the left anterolateral column, implicating Gowers' tract.

The resemblance to lumbothoracic syringomyelia in this case consists in the scars on the abdomen received in childhood as a result of painless burns; the preservation of tactile sensation, with almost complete loss of pain and temperature sensations in the lower limbs, although the degree of this

dissociation of sensation varied when the patient was at forced rest in bed; the extreme deformities of the knees, genu valgum, of five years' duration and resembling closely arthropathies; the slight exaggeration of the patellar reflexes, and the slight diminution of voluntary power in the lower limbs before the fall; the very slight kyphoscoliosis found only by careful examination; the absence of signs of psoas abscess, and of tuberculosis of the lungs before the accident, and the absence of a pronounced kyphosis. This, however, is not the first case of caries of the vertebræ without distinct kyphosis I have seen.

The attack of unconsciousness, with conjugate deviation of the head and eyes to the right, and the paresis of the left upper limb, developing a day or two before death, were the result of intense tuberculous cerebral meningitis.

The attempt has usually been made to explain the dissociation of sensation occurring in syringomyelia as a result of a cavity in the gray matter, or when this symptom occurs from other causes the lesion, whatever it may be, has been placed in the gray matter. This seems proper, because, so far as possible, we try to explain all the symptoms in a case by one lesion, although occasionally we err in so doing. A lesion in each anterolateral tract, if it involves the area in which the fibres of temperature and pain sensations are contained, must cause dissociation of sensation, just as truly as a lesion cutting sensory fibres crossing in the centre of the spinal cord, and the former is what has occurred in my case of caries of the vertebræ reported in this paper. The tract of Gowers is invaded by a tubercle on each side, which extends not much beyond this tract on each side, and this case seems to afford proof that Gowers' tract contains fibres of temperature and pain. We can understand why temperature and pain sensations are so often involved in the Brown-Séquard type of paralysis and tactile sensation escapes. The most common cause of spinal hemiplegia, which is of the Brown-Séquard type, is spinal syphilis, and the extension of the syphilitic inflammation from the pia into the peripheral areas of the cord and involvement thereby of Gowers' columns is of frequent occurrence. I believe that tactile fibres, at least in part, are in the posterior columns.

It seems very strange that after my patient had received a severe fall, had thereby become completely paralyzed in the lower limbs, and had been confined to bed, sensations for temperature and pain in the lower limbs should have improved during a brief period, although later they again became seriously affected. It may be that a few axis cylinders passed through the tubercles in the tracts of Gowers undamaged and became capable of transmitting some impressions for a time when the patient was at rest. The existence of normal axis cylinders within a tubercle has been shown. The spinal cord presents now diffuse degeneration, but this probably occurred after the severe fall the patient had, when he became entirely paralyzed. At the first examination I made, the lower limbs were not very weak, and the dissociation of sensation was typically syringomyelic in type, and was evidently caused by the two tubercles, one in each tract of Gowers, because these lesions are of long duration, and degeneration has occurred in the centre of each tubercle.

The severe fall, without causing fracture of the vertebræ, started a partially latent process and caused thereby complete paralysis of the lower limbs. The diffuse degeneration may, with propriety, be considered as of recent development, for it is especially intense in the crossed pyramidal tracts, but at my first examination very little weakness of the lower limbs was detected.

In a paper published in 1898 I[1] mentioned that Strümpell[2] takes a very decided stand in regard to the presence of meningomyelitis in Pott's disease. He says that all the changes in the spinal cord in spinal caries are only the necessary consequences of purely mechanical pressure. "At all events," he continues, "as we must state after numerous examinations made by us, in opposition to the prevailing view, no one has the slightest right to explain the paralysis occurring from spondylitis as the result of secondary myelitis."

If preparations are made from the spinal cord, there are, according to Strümpell, no vascular changes to be found, no hyperæmia, no accumulations of cells about the vessels, and only occasionally small traumatic hemorrhages. Frequently there are foci of degenerating nerve fibres, groups of swollen axis cylinders, with partial or complete loss of their medullary sheaths, and in places spaces from which the nerve fibres have disappeared. In later stages there is proliferation of the neuroglia.

Kraske[3] has expressed similar views in saying that the paralysis cannot be attributed to secondary inflammatory changes in the cord, and that this is equally true of the rare cases in which the cord is involved in the tuberculous inflammation, for this involvement occurs after the paralysis and toward the end of life.

I share the opinion that tubercular myelitis is not a common complication of caries of the vertebræ, but the case I reported in 1898 and the case that is described in my present paper are proof that occasionally it may occur.

[1] Johns Hopkins Hospital Bulletin, June, 1898.
[2] Lehrbuch der spec. Path. u. Ther., vol. iii. p. 197.
[3] Archiv für klin. Chirurgie, vol. xli.

A CASE OF AMYOTROPHIC LATERAL SCLEROSIS IN WHICH THE SYMPTOMS WERE UNILATERAL AND ASCENDING.

By Charles S. Potts, M.D.,
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In the University of Pennsylvania Medical Bulletin, January, 1905, vol. xvii. p. 390, Dr. William G. Spiller, in a paper entitled "Primary Degeneration of the Pyramidal Tracts: a Study of Eight Cases, with Necropsy," reported, among the others, two in which the symptoms were unilateral, and collected from the literature ten of a similar type. At the same time he commented upon the rarity of this form, and especially of those in which the progress of the symptoms was ascending. The following case was not included in the ten mentioned by Dr. Spiller, but was exhibited to the Philadelphia Neurological Society[1] in 1900; the history, however, was only very briefly given in abstract in the *Transactions* of the society:

J. D., aged forty-two years, a carpenter by occupation, but who had worked in a *lead works* for the past eighteen months, came to the dispensary for nervous diseases in April, 1900. There was nothing of significance in either his family or previous history, with the exception of his being exposed to lead, as above mentioned, and that nine months ago he had had severe pains in the stomach and constipation. Syphilis was denied.

Six months before coming under observation he first noticed weakness of the left leg and that the toes would catch in slight projections when walking. Several weeks after this weakness was noticed of the left arm, and very soon after this difficulty in swallowing and thickness of speech were manifest.

Examination. All movements of the eyeball and pupils were normal; the forehead could be wrinkled, but the lines of the lower part of the face were smoothed out. There was inability to whistle, and the angles of the mouth could not be drawn to either side with normal facility. The tongue was projected with difficulty and was somewhat atrophied. There was considerable difficulty in swallowing, especially solids. The uvula was deflected toward the left, but the soft palate could be elevated equally well on both sides. The speech was slurring, hesitating, and indistinct. Dr. C. P. Grayson reported that "the disturbance of the vocal cords and throat tended rather toward spasm than paralysis, but that motion of the right vocal cord was impaired."

All movements of both arms could be performed, but not with normal strength, the left being considerably weaker than the right. The dynamometer showed: right, 55; left, 30. Atrophy of the adductor pollicis and interosseii, with a claw-hand deformity, was present on the left side; there was a slighter degree of atrophy of these muscles on the right side. All movements of each leg could be performed, but with impaired strength, which was more marked on the left side. The patient walked stiffly and with short steps and dragged the left foot. The left leg was one-half inch less around the calf than was the right. The tendon-jerks were increased on both sides, ankle clonus and jaw-jerk being present, but were more so upon the left than the right. The Babinski reflex was also present on both sides. The skin reflexes were present and active. The urine could not be held as well as normally. All the muscles responded to the faradic current, but a much stronger current was required for the adductor pollicis and interosseii of the left and a slightly stronger for the same muscles of the right side. Fibrillary tremors and contractions were present in all museles, but were more marked upon the left side. The patient was emotional and laughed or cried without provocation. The sexual power was not impaired and sensation was normal. In this case, while both sides were affected, it is evident that the left became so first, and at the time of examination the patient was not aware that there was anything wrong with the right side. The bulbar involvement seemed to be bilateral, with the exception that the *right* vocal cord appeared to be weaker than the left. No distinct blue line was present upon the gums.

[1] Journal of Nervous and Mental Diseases, 1900, p. 556.

A CASE OF TUMOR OF THE LEFT FIRST AND SECOND FRONTAL CONVOLUTIONS WITH MOTOR AGRAPHIA AS ITS CHIEF LOCALIZING SYMPTOM; SUCCESSFUL REMOVAL OF THE TUMOR.

By J. W. McConnell, M.D.,

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(From the Department of Neurology of the University of Pennsylvania.)

Whether one is an extreme localizationist or not, the acceptance of certain facts regarding cerebral functions and their cortical representation has been forced by the presentation of pathologieal specimens proving such existences. Broca showed how a lesion of the foot of the left third frontal convolution produced motor aphasia. Ferrier, Horsley, and others established the until recently accepted geography of the region of the Rolandic fissure. In America the theories of Mills,[1] for the first time systematically presented in his paper of 1888, have advanced step by step to the views expressed in his most recent publications on cerebral localization,[2] in which are exemplified the convictions of a localizationist that sooner or later every portion of the cerebral cortex will be designated with its peculiar function.

Chiefest among the contentions of the opposing schools is the existence or otherwise of a motor graphic centre, or, as is suggested by Mills,[3] an executive writing centre. From a study of his paper on "Aphasia and the Cerebral Zone of Speech,"[4] one gleans the meaning of executive writing centre to be that portion of the brain in which are correlated all those cerebral functions which find their expression in writing. The rarity with which agraphia occurs as a separate and distinct symptom appears to be in the majority of instances the great objection to the acceptance of its localizing value. Until the weight of pathological evidence contributed is preponderant, such will be the case, and the report here submitted is toward the hastening of that end.

Case. S., white, American, carpenter, aged twenty-eight years, and married, has a negative family history. He never had convulsions in childhood, had few children's diseases; had a fall when eight years old, in which he struck the occiput, but suffered no consequences so far as is known. He denies all venereal diseases, is not a user of alcohol, and indulges only moderately in tobacco. He is right-handed.

His present condition dates from February, 1899, when, after a hearty meal, he had a convulsion, said to have been general. One year later he had a second seizure, followed in six months by a third; a fourth took place in December, 1900. In June, 1901, he had a series of attaeks, four in three days. These are described by his wife as follows: "He would shout, fall, and become stiff all over. In a moment he would commence to jerk, and, if not protected, would bite his tongue. After the jerking he slept, and on awaking complained of soreness of the whole body." These attacks lasted about ten minutes, were very frequent, and usually occurred at night. They were always succeeded by unconsciousness, but were not followed by paralysis, difficulty in speech, or any mental excitement. Occasionally while talking he would stop for a few seconds, look queer, then proceed with the matter in hand. The last series of general convulsions took place April 30, 1904.

On May 1, 1904, he had for the first time a convulsion without unconsciousness. So far as can be learned, it was limited to the right side of his face and consisted of "movements as though he was chewing." From that day he had no general convulsions, but many of these "spells" in a day and every day.

On May 18th five of these attacks within one hour took place under my immediate observation and were as follows: The patient, recognizing the oncoming of the attacks, walked across the room to where his brother was sitting. Before going two steps the right lower face was in clonic spasm, which quickly involved the right upper face and occasionally the rotators of the head to the right. The eyelids were in violent clonic spasm, but on forced separation the eyeballs were found not turned either to the right or left or up or down. Requested during an attack to make certain movements, the patient at once did so. The seizures lasted on an average eighty-five seconds, and were followed by mental confusion, and, judging from his appearance, a feeling of apprehension lest the attacks should again take place. He could correctly answer questions put to him immediately on the cessation of the spasm, but his replies were difficult to understand by reason of great thickness of speech, which disappeared within five or six minutes, at which time his talking was quite normal, and remained so until another attack occurred. He was admitted to the University Hospital May 18, 1904, having had twelve of the attacks just described within two hours. This rate of frequency continued to the day of the operation, with slight change.

[1] Cerebral Localization in its Practical Relations. Transactions of the Congress of American Physicians and Surgeons, 1888.

[2] Journ. Amer. Med. Assoc., Oct. 4, 1902; Medical News, N. Y., Nov. 5, 1904; Univ. of Penna. Med. Bulletin, May, 1904.

[3] The Nervous System and its Diseases, Phila., 1898.

[4] Aphasia and the Cerebral Zone of Speech. American Journal of the Medical Sciences, Sept. 1904.

Examination by Dr. Charles K. Mills, Dr. W. G. Spiller, and myself, May 19, 1904, showed no paresis or paralysis of any muscle or group of muscles of either the upper or lower extremities. He had neither static nor motor ataxia; all the movements of the arms and of the legs could be instantly and properly performed.

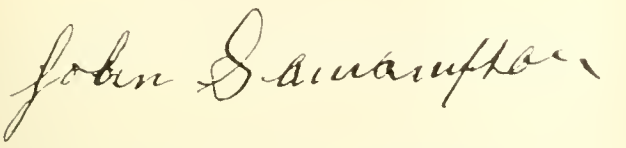

Fig. 1.—Attempt to write his name, May 18, 1904.

The right face was somewhat paretic in its lower half. The eyelids of the right side could be more readily separated by the examiner than those of the left side. When the eyes were open the right upper lid was not retracted as fully as the left, and on effort to widely open them the right levator palpebræ was aided by overaction of the occipitofrontalis. Forcible closure of the eyes caused deeper furrowing of the left than of the right face. These motor conditions were all intensified after a spasm and were regarded as exhaustion phenomena, the patient having had seventy-one attacks since admission to the hospital.

Sensation to touch and pain seemed to be less acute on the right face, the difference being estimated by the wincing of the patient during the examination. There were no sensory changes in the limbs or trunk, no astereognosis. Reflexes were apparently normal.

Speech was very thick, but by careful attention what he said could be made out. The patient recognized this difficulty and would endeavor to speak more distinctly by separating each word, thus: I—can—talk—better—after—while. The speech defect was a paresis of the articulatory, enunciatory, and phonatory apparatuses rather than an aphasia due to lesion of Broca's region, and was rapidly growing worse. Two days before it was noticeable only after spasms, but at our examination it was constant. It was not confined to any word, words, letter, or letters. Labials, dentals, linguals, gutturals, all were equally affected. He had no difficulty in reading print, writing, or numbers, or in recognizing and correctly naming objects.

He was asked to write, but the specimen was largely a series of meaningless strokes. The pencil was properly held and well managed, but efforts were fruitless. The result was the same on attempts at spontaneous writing or from dictation (Figs. 1 and 2). Writing from copy was practically perfect. A letter written two years before coming under observation showed omissions, faulty spelling and formation of words and letters in one part, which words were elsewhere spelled correctly or the letters properly formed. Specimens of later date showed an exaggeration of these conditions up to the point of complete inability to write, as evidenced in the specimen of May 19, 1904.

Examination of his eyes by Dr. G. E. de Schweinitz was negative, except that he was blind in the right eye from local causes.

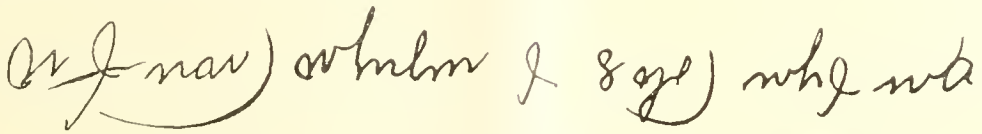

Fig. 2.—Attempt to write "when I was eight years old" from dictation, May 19, 1904.

From his wife it was learned that for over a year the patient's mental condition was changing. He was irritable and seemed less able to understand than formerly. He complained that he could not remember what he read from day to day. In telling familiar facts he would have to stop and think what to say; he often said he could not think as fast as he could talk. His difficulty seemed to be to continuously fix his attention and keep his mental machinery in action. As his convulsive attacks became more frequent, his memory for recent events became more and more impaired.

He never had any delusions, never any hallucinations of sight, hearing, or smell.

He was operated upon by Dr. Charles H. Frazier on May 21, 1904, an osteoplastic operation being performed. The flap as originally marked out had a base of two inches; it was three inches long and three inches wide at its upper, broadest part; the line of the fissure of Rolando passed through the centre, thus giving one and one-half inches in front and the same behind the full length of the central fissure. Previous to the operation the position of the flap was tilted so that the base line was parallel with the fissure of Sylvius and the anterior margin of the opening was two inches in front of the line of the central fissure.

Before opening the dura visible pulsation was barely perceptible. There was a marked groove in the dura near the line of the Rolandic fissure. Faradic stimulation of the unopened dura produced no response. On opening the dura an intensely congested area was observed in the anterior and superior portion. This proved to be a tumor mass. It was superficial and, after enlarging the bony opening forward and upward, was entirely removed. It lay across the foot of the second frontal convolution, encroaching somewhat on the lower half of the first, slightly upon the upper posterior portion of the third frontal convolutions and the anterior edge of the precentral convolution.

Faradic excitation of the cortex was employed, and is described in the paper of Drs. Mills and Frazier in the present issue of the UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN (July and August, 1905) as Observation 1.

Recovery from the operation was good. There was some paresis of the right lower face, greater than before the operation, and some weakness in the right hand. Speech was immediately better, but the agraphia persisted, as can be seen in the specimen of June 1, 1904 (Fig. 3). This, however, gradually improved, so that June 12, 1904, he wrote a letter of over a page, of good construction, and almost perfect spelling. The wonderful improvement is evidenced by the specimen (Fig. 4).

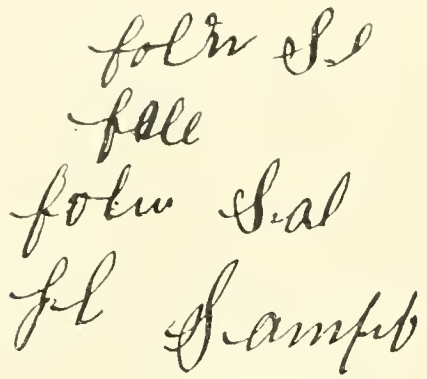

FIG. 3.—Attempt to write his name, June 1, 1904.

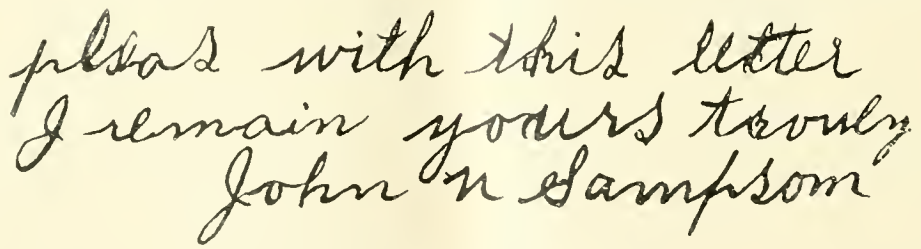

FIG. 4.—Part of a letter written June 12, 1904.

He left the hospital June 12, 1904, apparently well on his way to absolute recovery.

In 1856 Marcé[1] stated "that the centres of co-ordination for spoken and written words are different and separated from each other in position. Ability to write is independent of the mobility of the hand, since when the hand has preserved all its powers writing has been proved to be impossible." Years after Marcé's observation Ogle,[2] noting the great difference, in some instances, in the loss of speech and the defect of writing ability, introduced for the latter condition the term agraphia. From this time to the report by Gordinier[3] of his case of pure motor agraphia arguments have been proffered in favor of and against the importance of agraphia as a localizing entity and the existence in the left second frontal convolution of an executive centre for writing. Gordinier's study is so complete that but a few cases will be cited in this presentation and some of these are quoted by him.

Dejerine[4] maintains his belief that the motor speech centre is capable of acting as executive for both spoken and written speech and that if a motor graphic centre did exist its destruction would abolish the possibility of executing any kind of writing. Such a theory follows the teachings of Trousseau,[2] who was a firm believer in the parity of speech and writing loss in lesions of Broca's centre. Cases to support these views can be found in numbers, but without exception the pathological condition found has been a lesion or lesions involving the left third frontal convolution in its entirety and invading surrounding gyres.

On the other hand, cases of aphasia without agraphia have been reported wherein postmortem the foot of the left second frontal convolution was not at all involved. Such a one is reported by Mills,[3] another by Ogle.[4] An interesting record is that by Oppenheim[5] of a patient with pure motor aphasia, who was able to write and paint during his entire illness of seventeen years.

The cases heretofore reported of pure motor agraphia are few in number, but give some weight to the evidence in favor of the existence of a motor graphic centre. The case of Charcot and Dutil,[6] observed for years, was originally one of motor agraphia due to an apoplectic seizure. Years later a second attack resulted in motor aphasia, and still later repeated apoplexies caused death. At autopsy what seemed to be the oldest focus of disease was in the foot of the left second frontal convolution. The left third frontal gyre was also involved by a second separate focus of softening, and several foci were found in the right hemisphere. This seems to be the earliest reported case which gives grounds to localizationists for their contention.

[1] Compt.-rend. des séances et mémoires de la Soc. de biol., 1856.

[2] St. George's Hosp. Rep., 1867, vol. ii.

[3] Amer. Journal of the Medical Sciences, May, 1899, and Sept., 1903.

[1] Compt.-rend. Soc. de biol., July, 1891.

[2] Lectures translated by Bazire, 1886, p. 221.

[3] Aphasia and the Cerebral Zone of Speech. American Journal of the Medical Sciences, Sept., 1904.

[4] St. George's Hosp. Rep., vol. vii. p. 105.

[5] Diseases of the Nervous System, translated by Mayer, 1900.

[6] La france médicale, 1878, p. 609. Mém. de la Soc. de biol., 1893, p. 129.

The patient in the case reported by Eskridge[1] could not write spontaneously, but could copy and write if words were spelled for him. An operation evacuated a cyst in the left second frontal convolution.

Gordinier's[2] case of lesions of the left second frontal convolution which produced complete agraphia without aphasia of any variety is the only example of its kind up to the present time. In the discussion of it he cites Collins to this effect: "The ideal case to prove the existence of a centre whose function is to store graphic images and whose destruction would cause agraphia would be one in which there was inability to write spontaneously and from dictation, and in which no disturbance of motility, particularly of the right upper extremity, no aphasia, no alexia, no verbal deafness, and no verbal blindness existed."

The case here reported seems to fulfil the requirements of Collins and to prove that motor agraphia is an entity of localizing value and that it is due in right-handed persons to a lesion limited to the foot of the left second frontal convolution.

[1] Medical News, Phila., Aug. 1, 1896.

[2] Amer. Journal of the Medical Sciences, May, 1899, and Sept., 1903.

A STUDY OF THE CONTRACTURES IN ORGANIC NERVOUS DISEASES, AND THEIR TREATMENT.

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(From the Neuropathological Laboratory of the University of Pennsylvania and the Philadelphia General Hospital.)

One of the most interesting problems in neurology is the cause of the contractures in the various forms of nervous disease. Much has been written upon this subject, and yet, in spite of this, we are in possession of only a very few facts. Almost every writer upon this subject has advanced a new theory, little better, however, than those previously held.

The study of contractures was undertaken with the view of considering this interesting problem, and especially to determine clinically the nature of the contractures in the different nervous diseases.

Approximately about 500 patients were studied, these being mostly in the nervous wards of the Philadelphia General Hospital and in the Philadelphia Home for Incurables. I wish to thank Drs. H. B. Calhoun and R. Pemberton, the resident physicians in the former, and Dr. Wm. Fox, the resident physician in the latter institution, for their help.

Contractures may be either passive or active. By passive contracture is meant a condition due to disease of the part, as joint disturbances, inflammation of the parts around a joint, the muscle diseases (paralysis agitans probably comes under this class as being largely a muscle disease), and the contractures which are the result of faulty positions and of paralysis of the antagonistic muscles, as, for instance, in multiple neuritis and anterior poliomyelitis. The contractured limbs can be moved passively very little, if at all, and the contractures are not influenced by foreign conditions such as heat and the time of day, and do not disappear during sleep or in ether narcosis.

Active contractures are always due to a disease of the central nervous system in contradistinction to the passive contractures which do not always have such an etiology. Passive movement is always possible in the former, although it is slow. The intensity and the extent of course vary in the different diseases. During sleep and in ether narcosis, as I have seen, the contractures disappear, providing no structural changes are present. They are less in the morning and in warm weather, and any emotion or movement will increase them. Passive contractures may in addition appear, due to structural change.

The contractures present in cerebral diseases will be considered first. Recently, in a clinical study of hemiplegia, 160 adult cases were observed. Since then 24 cases have been added, this making a total of 184 adult hemiplegics. With Dr. Spiller I have also had the opportunity of studying 26 cases of infantile hemiplegia in the Pennsylvania Training School for Feeble-minded Children at Elwyn. To this number six similar cases seen in other clinics may be added, making a total of 184 adult and 32 infantile hemiplegics observed.

Todd[1] assumed that there were two forms of contractures in hemiplegia, the early and the late. The early contractures, according to him, may come on immediately after the onset of the hemiplegia, or a few days after, and last only a very short time. The late contractures appear about from the second to the sixth week after the development of the hemiplegia and are permanent. Gowers,[2] however, makes another and better classification. He calls "initial rigidity" the condition appearing directly after the onset, this lasting only a few hours. He accepts the "early rigidity" of Todd appearing a few days after the stroke and lasting a few weeks, also the "late rigidity" coming on in the course of some weeks and remaining permanently. He also distin-

guishes an ultimate "structural contracture" from the late rigidity.

According to von Monakow[3] the early contractures consist in a sudden tonic cramp of a group of muscles, or of all of the muscles of one or both extremities of one side. They may assume any form, and sometimes it is difficult to distinguish them from hysterical contractures. As a rule, however, they assume the position of late contractures. At times a clonic tremor may precede the early contracture.

I have never been fortunate enough to observe a patient in the onset of a cerebral hemorrhage, but have seen at least three patients within a few minutes, and a number several hours after such an occurrence, but have never seen the so-called initial rigidity. I have, however, observed rigidity in the muscles of the paralyzed side some days after the attack, and in one instance clonic movements about six hours after the stroke. The latter were supposed to be due to a ventricular hemorrhage, but at the autopsy such a condition was not found; the lateral ventricles, however, were a little dilated with cerebrospinal fluid, this being especially marked on the side opposite the hemiplegia.

Duchenne[5] explained the early contractures as being due to an inflammatory process in the limits of the hemorrhagic lesion, and other authors, by a ventricular hemorrhage. I have so far observed four cases in which it was thought that a ventricular hemorrhage caused an irregular tonic-clonic spasm. One was in the case mentioned above; in the second the hemorrhage did not extend into the ventricles, and in the other two no lesions were found, the hemiplegia probably being uræmic in origin. It is rather doubtful that either the early contractures or the clonic-tonic spasms following an apoplectic attack are always due to a ventricular lesion.

More probably the same cause which partially interrupts the continuity of the motor fibres may cause an irritation, for it has been shown that irritation of a nerve may cause contractures or total flaccidity, depending upon the amount of irritation. Of course it is not to be expected that early contractures or clonic spasms could appear in a total destruction of the motor fibres. The extrapyramidal tracts are so little developed in man that they could hardly assume an immediate function. It seems probable that if early contractures appear, the motor tracts are not totally cut off, and therefore we may give a better prognosis. This is an important point, and has not been before called attention to.

The variable nature of the early contractures can be explained by the fact that the irritation is probably an abortive one and is soon exhausted. Besides, most of the motor fibres have been cut off, and an impulse would therefore be insufficiently carried and would be diffused to irregular groups of muscles.

The late contractures appear between the second and the sixth week, although in one of my cases, in which the return of power in the lower limb returned about the second month, there were no signs of recovery in the upper limb until about six months after the attack, when flexor contracture developed in the fingers. The late contractures are permanent.

As a rule the hemiplegic contractures always assume the same type and are in flexion in the upper limb and in extension in the lower. The arm is adducted and held closely to the side of the chest, the elbow is flexed, the forearm pronated, the wrist turned inward, and the fingers are flexed strongly. In the lower limb the leg is held in extension and the thigh is either adducted or, more rarely, abducted, and the foot is in the position of talipes equinovarus. The toes are flexed, although occasionally the large toe is permanently extended. This is the usual contracture both in the adult and the infantile forms.

Fig. 1.—Flexor contracture in spinal syphilis, showing permanent extension of large toes.

Of course contractures vary greatly in their intensity. In some cases they are entirely absent, there being simply a stiffness or rigidity which has been so aptly called the "imminence of contracture."

One of the most common variations from the usual form is where the arm is not held rigidly to the side, but more common still are those cases in which the fingers are extended. The power of extension, however, is never equal to that of flexion. Extension of the fingers is more common in infantile hemiplegia, for in the 32 cases studied extension of the fingers was possible in 13, while of the 184 adult hemiplegics the fingers were extended only in 9. Sometimes the hand is acutely deviated outward. This I have not seen in the adult type.

The contractures of the lower limb are fairly constant.

The thigh is more often adducted than abducted, but not so often as most authors hold. In fact, in nearly one-half of my adult cases abduction of the thigh was present. The foot is always in the position of talipes equinovarus.

In rare cases the sternocleidomastoid and the platysma myoides muscles are contracted. More rarely the face is involved and even the tongue has been found to deviate to the healthy side in contracture. The chest and abdominal muscles are hardly ever involved.

We shall now consider the bilateral contractures due to cerebral disease, either as the result of unilateral or bilateral lesions. Spiller[5] recently recorded a case in which bilateral contractures were present due to a unilateral lesion, and states that this condition seemed to be unknown outside of the French school. He referred to cases recorded by Hallopeau, Brissaud, Pitres, Dignat, and Féré. I did not find a single instance in the cases studied by me of what could be considered bilateral contractures due to a unilateral lesion. A slight amount of stiffness and rigidity was found in the limbs of the "sound side," but never contractures.

I have observed 5 cases in which the clinical picture was that of a hemiplegia with contracture of the leg of the "sound side." At necropsy, in 2, lesions were found in each lenticular nucleus, with involvement of the pyramidal fibres; in 1 there were multiple areas of softening in the brain and cord; 1 proved to be a triplegia with a degeneration of both pyramidal tracts, and in the last case, a tumor, probably a sarcoma, was found invading one frontal lobe and involving the motor fibres of both sides through pressure.

Brissaud[6] considered bilateral contractions from unilateral lesions as relatively common, but others, as Dignat,[7] regarded them as rare. It is even stated that such conditions may appear in the course of an adult hemiplegia, as in a case of Dignat in which a man of eighty-seven years of age developed bilateral contractures after the hemiplegia existed for a year.

In all of the descriptions of such conditions it is noted that the thighs are strongly flexed upon the abdomen and the legs on the thighs and that the upper limbs are contracted in flexion. It is difficult to understand why contractures should develop in the "sound side" in a hemiplegia from a unilateral lesion. Should such contractures take place, why should they assume an entirely different form, in flexion in the lower limbs, when the usual form of hemiplegic contractures is in extension? Bilateral flexion contracture, such as has been described as occurring in this disease, is usually found as a result of bilateral cerebral lesions, as, for instance, in the 5 cases observed by me and cited above, or as a result of spinal-cord lesions.

With the exception of Spiller's case, all of the recorded instances were studied prior to 1883, before modern methods were in vogue, and it is probable that a careful study would have shown, at least in the adult cases, bilateral cerebral lesions probably as a result of multiple areas of softening due to arteriosclerosis.

It must not be forgotten that at times there may be a coincident arteriosclerotic neuritis in the lower limb of the "sound side," this giving the appearance of bilateral contracture due to a unilateral lesion. Such a case was recently reported by Burr and Camp.

Spiller's case was due to a unilateral hydrocephalus, which was either congenital or acquired early in life. Both the upper and lower limbs of each side were markedly contractured in flexion, but those of the side opposite to the lesion much more intensely. No lesion was found in the opposite hemisphere. Spiller says: "The explanation for the bilateral hemiplegia is to be found in the innervation of both sides of the body from each side of the brain. There can be no doubt that each cerebral hemisphere innervates both sides of the body, but the fibres innervating the so-called sound side are fewer in number, and therefore the contracture on this side, when it occurs, is less intense than in the more paralyzed side, and this was the condition in my case."

This case was very carefully studied, serial sections being made through the diseased cerebral hemispheres, but no lesion was found in the other hemisphere. It is well known that in lesions which are either congenital or acquired in early life it is difficult and almost impossible to demonstrate secondary degeneration, even by the Weigert method, because of compensatory growth of fibres. Spiller found the pyramidal tract associated with the diseased cerebral hemisphere to be much smaller, both in the pons and medulla oblongata, than the pyramidal tract of the other side, and the degeneration in these areas and in the spinal cord was very slight. The crossed pyramidal tract of the so-called healthy side appeared a little less deeply stained by the Weigert hematoxylin method than the surrounding parts of the anterolateral column.

Dr. Spiller has personally expressed to me the opinion that the motor fibres from the apparently healthy hemisphere may have been imperfectly developed, and this may be the explanation for the contractures in the so-called "sound side."

The assumption that a sufficient number of fibres innervate the body on the same side as the cerebral hemisphere in which they arise, and that these cause the contracture of the limbs of the sound side, at least so far as the adults are concerned, is not tenable, because if this were so we should certainly find such contractures more frequently. As stated above, of 184 adult hemiplegics studied no such instance was found.

We can conclude therefore that a unilateral cerebral lesion in an adult cannot cause bilateral contracture, and that bilateral contractures in the adult are always due to bilateral cerebral lesions.

The form of the contractures due to bilateral cerebral lesions seem to vary according to the nature and the time of life the injury was sustained; thus the clinical picture and the contractures differ in the cases in which the lesions occur either before or at birth and in those in which they occur in the adult.

It is unfortunate that so much confusion still exists as to what diseases should be included under the title of Little's disease. According to Spiller,[8] cases of congenital spastic rigidity without paralysis, cases with paralysis, cases with epilepsy, cases with feebleness of intellect, cases resulting from injury of the brain at birth, cases resulting from premature birth, and cases of cerebral and spinal lesions are designated as Little's disease.

In a number of the subdivisions enumerated under this head a certain form of contracture has become so well known that it has been designated as typical of Little's disease. In this form the lower limbs are always involved, while the upper may or may not be contractured. The thighs are partially flexed on the abdomen, and are strongly adducted and rotated inward. The knees are bent and the feet are in the position of talipes equinovarus. If the upper limbs are involved, the contractures are usually in flexion, although the arms may be held away from the chest and the fingers extended. The contractures in all the conditions referred to by Spiller are the same, except in the cases of cerebral diplegia.

In this condition all of the limbs are usually contractured, and about equally so, differing from the former classification, in which the upper limbs are usually not at all or only slightly involved. The contractures in the upper limbs in diplegia are the opposite to those in hemiplegia. The arms are held away from the chest, the elbows are flexed, the forearms are supinated, and the wrist and fingers are extended. In the lower limbs the contractures resemble those found in the other forms of Little's disease, except that they may be more marked. In diplegia athetosis and other movements are very common.

Should bilateral cerebral injuries or lesions occur after the full development of the pyramidal tracts, we would have the well-known picture of pseudobulbar palsy. Even here the clinical symptoms would differ somewhat in the young and in the adult, for the lesions would be dissimilar. The usual cause of adult pseudobulbar palsy is an arteriosclerosis of the cerebral vessels, causing multiple areas of softening, while in the young congenital lesions, multiple cerebral tumors and injuries are the most common causes.

In the adult form of diplegia the lower limbs are usually weaker than the upper, in opposition to the rule in hemiplegia. Severe contractures are rather unusual, the limbs generally being rigid, but in exceptional cases the contractures are marked. Thus in one case with autopsy both the upper and the lower limbs were in marked flexor contracture.

It may be said, therefore, that whenever bilateral contractures occur, no matter what the lesions or the time of life they developed, the contractures both in the upper and lower limbs are always in flexion.

We will now consider the causes that lead to the contractures in cerebral disease. Of the many hypotheses which have been advanced, only the more important will be mentioned. The early authors, as Todd and others, believed that the irritation of the lesion itself caused the contractures of hemiplegia. Later Bouchard[9] thought that the degeneration of the pyramidal fibres caused an irritation of the spinal cord. Charcot,[10] going a step farther, believed that the irritation was exerted on the nerve cells of the anterior horns of the spinal cord, this causing an increased tonus and contracture. Still others believed that the influence of the sound hemisphere was the responsible factor, while Hitzig[11] was of the opinion that the contractures were no more than involuntary associated movements.

Of the authors of more recent date, Mann[12] is of the opinion that there is a close relation in the brain of the fibres for the agonistic and antagonistic muscles, and that in a hemiplegia only certain muscles or muscle groups are involved, while others are very little if at all affected. He assumes that in the pyramidal tracts there are fibres which transmit, besides the irritative impulses for certain muscle groups, inhibitory impulses for their antagonistic muscles, and the greater implication of the inhibitory fibres causes a state of hypertonia in hemiplegia.

Lazarus,[13] in opposition to Mann, believes that the cause of the contractures in hemiplegia is the total destruction of the pyramidal tracts, and not a partial destruction. The more the destruction, the greater the paralysis and the contracture. He also, in opposition to Mann, showed that the antagonistic muscles were also paretic. Lazarus also believes that the hypertonia is a purely muscular phenomenon.

Some authors, as Van Gehuchten,[14] are of the opinion that the pyramidal tract has a depressing action on the muscle tonus and the reflexes, and assume that tracts leading from the cerebellum to the spinal cord, the so-called cortico-pontile-cerebello-spinal tracts, have an irritative action. Hence in a lesion of the pyramidal fibres impulses travel by means of these cerebellar tracts, causing a hypertonia. There is, however, no anatomical proof of such tracts.

Von Monakow,[15] supported by Oppenheim[16] and Rothmann,[17] advanced the theory that in the cutting off of the normal pyramidal fibres the sensory impulses are projected upon the lower motor apparatus in the pons and optic thalamus, and that the resulting action of this subcortical centre causes the partial return of function in the paralyzed limbs and the contractures. Von Monakow accepts the teaching of Exner and Sternberg, viz., that there are in the central nervous system excitomotor as well as depressomotor fibres,

and by irritation of the former the muscular tonus may be exaggerated and contractures result. Therefore, according to him the contractures are the result of the function of the subcortical centres assisted by (providing that the pyramidal tracts are not totally destroyed) the irritation of the excito-motor fibres.

Parhon and Goldstein[18] found atrophy in the paralyzed side in association with the contracture, and believed that the presence of the atrophy had a possible relation to the contracture. This is probably not so, because, as has been shown by Marinesco,[19] myself,[20] and others, atrophy invariably accompanies hemiplegia, whether there is contracture or not.

It is well known, chiefly through the work of Wernicke and L. Mann, that in a permanent hemiplegia the recovery of function takes place in certain muscle groups whose functions are synergic. This is as we should expect, because movements instead of muscles are represented in the cortex, and a destruction either of the motor cortex or of the fibres coming from it should cause paralysis of motion, and partial recovery should cause return of motion.

It is an interesting fact that if we compare the position of the contractured limbs in a hemiplegia, it will be found to be identical with the position most commonly assumed by an adult when at rest. In a normal person there is always a certain excess of strength and tonicity in certain groups of muscles as compared with their antagonists, as shown, for instance, in the greater power of flexion of the fingers than of extension, and of adduction of the thigh than of abduction.

The nature of the hemiplegic contracture coincides with this physiological relation. Directly after an apoplectic attack all of the muscle groups are paralyzed. As function returns, the stronger muscle groups have a greater return to power, thus causing the contracture.

The best explanation for the return of function in the paralyzed limbs after a destruction of the pyramidal fibres is probably found in the influence exerted by the extra-pyramidal tracts. These are well developed in the lower animals, and as has been shown, especially by Rothmann, experimental cutting of the pyramidal fibres causes hardly any loss of power, even in the higher anthropoid apes, because of the function of the extrapyramidal tracts.

These extrapyramidal tracts consist of the tract leading from the anterior corpora quadrigemina to the spinal cord, and of von Monakow's bundle, which runs from the red nucleus to the spinal cord. Their cerebral connection has not as yet been anatomically demonstrated, but it probably exists.

According to Rothmann, after a hemorrhage, these tracts are unable at first to cause any return of power, but their influence is sufficient to bring back the tendon reflexes. After some weeks the developing motor function of the optic thalamus and the corpora quadrigemina are of sufficient strength to cause the permanent return of power, and hence the contractures.

The nature of the bilateral contractures in bilateral lesions can be explained through mechanical grounds. As has been previously mentioned, they are always in flexion both in the upper and in the lower limbs, but the contractures in the upper limbs are more often absent. There is no organic reason why, in bilateral lesions of the motor tracts, the contractures should assume a different form than in a unilateral lesion. When a lesion of the pyramidal tracts occurs the same type of paralysis should ensue.

Assuming, then, that in the lower limbs the paralysis is always greater in the flexors, how are we to explain the resulting flexor contracture? If such a person is compelled to remain in bed, he will invariably flex his thighs on his abdomen and the legs on the thighs, because he is more comfortable in that position. Because of the persistence of this position the contractures will naturally assume permanent form, this being aided somewhat later on by structural changes. The contractures in the upper limbs are always in flexion, whether the lesion is unilateral or bilateral, not only because the flexors are stronger, but also because this is the most comfortable posture for these limbs.

Very rarely the usual hypertonicity which accompanies hemiplegia remains persistently absent. This absence is always accompanied by failure of return of power in the paralyzed limbs and absent reflexes. As a rule, destruction of a pyramidal tract causes hypertonia and increased reflexes in the paralyzed limbs, but some authors, as Rothmann, believe that only increased reflexes result, while the tonus may or may not be affected. A discussion of the various theories regarding the presence or absence of tonus will not be entered into; it will suffice to say that, in the opinion of most neurologists, degeneration of the pyramidal tracts causes hypertonia and increased reflexes.

If the return of power in the paralyzed limbs is dependent upon the function of the extrapyramidal tracts, a destruction of these tracts, in addition to a destruction of the pyramidal tracts, should cause permanent loss of power with flaccidity and lost reflexes. Pathological evidence as shown by the instances reported by von Monakow, and lately by H. v. Alban and M. Infeld[21] support this view. The prognosis in these cases is necessarily grave.

Assuming that destruction of the extrapyramidal bundles causes hypotonia, and that the normal functioning of these tracts causes a partial return to power and a certain amount of hypertonicity, an irritative lesion of the extrapyramidal tracts should cause an increased amount of hypertonicity in the affected limbs. Such a condition was first described by v. Bechterew[22] in 1900, who, under the title of "Hemitona Apoplectica," reported three cases. Spiller[23] soon after

observed a similar case, and applied the much better title of "Hemihypertonia Postapoplectica" to this condition. McCarthy[24] and Pfeiffer[25] have since reported similar instances. Two cases, not entirely typical, were studied by Dr. Spiller and myself at Elwyn. Briefly, their clinical histories are as follows:

Case I.—L. H., girl, intelligent, aged nineteen years, had convulsions when teething, and has been paralyzed on the left side since. Movements of the left upper limb are possible in all directions, but are somewhat impaired. Flexion of the fingers of the left hand is fair, but extension is much impaired. She drags her left lower limb when walking, but movements of the limb are fairly well performed. Flexion of the left foot is quite good, but there is no power of extension.

Voluntary movement of the paretic hand causes an irregular rotatory movement of the hand and fingers which resembles somewhat athetoid movements, but are more rapid. The spasms are only apparent in voluntary movement and last a very short time, therefore the case is atypical. These movements are also present to a limited degree in the toes and foot of the affected side.

Case II.—K. M., girl, imbecile, aged nine years, had convulsions at fifteen months and is epileptic. She has a right hemiplegia, which evidently has been present since early childhood, probably appearing at the same time as the convulsions. The right upper limb is contractured in flexion at the shoulder and elbow, but this contracture can be easily overcome. There is considerable power of flexion present in the right hand and slight power of extension in the right wrist, but extension of the fingers is impossible.

When first examined the fingers of the right hand were flaccid and could be overextended, but manipulation of the limb caused a marked contracture of the fingers which after a few moments disappeared, the fingers again becoming flaccid. Voluntary movement brought on the same condition of spasm, followed by a temporary flaccidity.

The right lower limb was contractured in extension, there being no movement possible in the foot or toes. This case is atypical in the degree of paralysis, and in the manifestation of hypertonia only after active or passive movement. In typical cases of postapoplectic hemihypertonia, the loss of power is not very great. The intermittent tonic spasm affects different groups of muscles and differs from athetoid movements. The hypertonicity may come on directly after the hemiplegic attack or not for some years.

CONTRACTURES IN SPINAL-CORD DISEASES.

The nature of the contractures in diseases of the spinal cord depend upon the seat of the lesion. Thus we may make three subdivisions: first, those cases in which the cells of the anterior horns or their roots are diseased; second, those in which the pyramidal tracts are involved; and third, those in which there is a lesion involving both the cells of the anterior horns and the pyramidal tracts.

In the first subdivision may be placed the poliomyelites, both of childhood and adult life, and progressive spinal muscular atrophy. As the paralysis in anterior poliomyelitis may involve irregular groups of muscles in one or all of the limbs, and the palsy is flaccid, the contractures which develop are due to the action of the non-paralyzed muscles and are passive in character.

In progressive spinal muscular atrophy the contractures depend upon the paralysis of some muscles before their antagonists are affected. Thus the claw-hand is dependent upon the paralysis of the interossei and the contracture of their antagonists, the extensor muscles of the fingers. Contractures may develop in the feet, but, as a rule, death occurs before they become involved.

In the second subdivision are the primary degenerations of the pyramidal tracts. In this disease the contractures are similar to those seen in hemiplegia, viz., in flexion in the upper limbs and in extension in the lower. There is, however, this difference, that the upper limbs are not usually so much contractured as in hemiplegia, and the lower limbs are more involved than the upper. This is no doubt due to the difference in the nature of the lesion. While in both we have a degeneration of the pyramidal tracts, in one it is the result of a sudden destructive lesion, in the other it is a primary progressive degeneration. Degeneration of the pyramidal tracts should ultimately give the same symptoms, no matter what the etiology, but in the primary form the symptoms are of such slow progress that the patient learns to adapt his movements to his pathological condition, this being seen especially in the arms, with the result that the paresis and the contracture in the upper limbs are never so marked as in the much less controlled and coarser-moving lower limbs.

In the latest stage of this disease, after the patient has become bedridden, the extensor contracture in the lower limbs may alter into flexion. This is no doubt due to mechanical causes, such as the position in bed and the natural tendency to flex the limbs while at rest.

In the third subdivision may be included the remaining system diseases, as amyotrophic lateral sclerosis, and all of the organic diseases of the spinal cord, which involve both the cells of the anterior horns of the spinal cord and the pyramidal bundles. Such diseases are the diffuse sclerosis, multiple sclerosis, Friedreich's ataxia, syringomyelia, and the different forms of myelitis.

The contracture of amyotrophic lateral sclerosis is so much like that described as occurring in primary degeneration of the pyramidal tracts that a separate description is not necessary. There is this difference, however, that in the

former there is the accompanying atrophy due to the disease of the cells of the anterior horns, and that the upper limbs are about as much involved as the lower. Because of this atrophy the contractures are more marked, and in the upper limbs resemble very closely the contractures of hemiplegia.

The contractures of the remaining diseases included under this class depend largely upon the relative involvement of the motor fibres and of the nerve cells of the anterior horns. A lesion involving both of these areas will almost always produce flexor contracture. This is largely due to the atrophy caused by disease of the nerve cells and to mechanical influences.

It seems to me that the influence of mechanical causes—as the pressure of bed-clothes and the position of the patient in bed, and the physiological tendency of the patient to draw up his thighs and legs, especially if there be any pain or cramp in these members—has not been sufficiently recognized as a causative factor of contractures.

CONTRACTURES IN DISEASES OF THE PERIPHERAL NERVES.

In this class are included multiple neuritis, disease of individual nerve or nerves, and primary neurotic atrophy. It can be readily understood that the contractures are passive and are dependent upon the action of the non-paralyzed muscles. In early primary neurotic atrophy, because of the peroneal palsy, the foot assumes the characteristic position of foot-drop.

Sometimes secondary contraction occurs in the distribution of a paralyzed nerve, as, for instance, in old facial paralyses; when this happens it is difficult at first sight to recognize the facial palsy. The secondary contracture is probably due to changes in the muscle.

CONTRACTURES IN MUSCLE DISEASES.

The muscular dystrophies and, for convenience, paralysis agitans will be discussed here. Of course the contractures in the muscular diseases are dependent upon the groups of muscles paralyzed, the contractures being passive. It is hardly necessary to discuss these further.

The cause of the symptom-complex, known as paralysis agitans, still remains unsolved. The form of its contracture is well known, and yet it remained for Spiller[26] to point out last year the marked resemblance in the contractures between this disease and arthritis deformans. He called attention especially to the tendency for ulnar deviation of the hand in paralysis agitans, a symptom invariably present in rheumatoid arthritis.

In an examination of fourteen cases of paralysis agitans ulnar deviation was found in eleven. In one patient studied in the Philadelphia Home for Incurables, and whose picture is given, the attitude and contractures were so much like

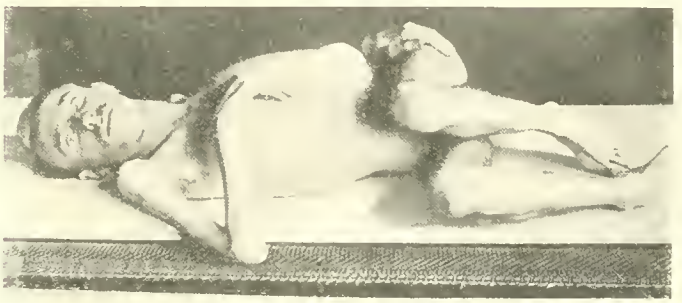

Fig. 2.—Contracture in muscular dystrophy.

those of arthritis deformans that it was not until the tremor was demonstrated that paralysis agitans could be diagnosticated.

Fig. 3.—Paralysis agitans with contractures resembling those of arthritis deformans.

There can be no doubt of the correctness of Spiller's observation. McCarthy has recently also substantiated his views.

THE TREATMENT OF CONTRACTURES.

The contractures of hemiplegia will be first considered. Manifestly, if the contractures are due to the better recovery of some groups of muscles over others, the proper treatment

would be either the strengthening of the weaker muscle groups or the prevention of overaction by the stronger muscles.

There is no doubt that contractures can either be totally prevented or ameliorated to a large degree if treatment is applied properly and is started early in the disease, before structural changes take place. Unfortunately, it is almost impossible to properly care for the large number of hemiplegics who frequent the nervous wards in the large hospitals, as, for instance, in Blockley, and we have become accustomed to expect more or less marked contractures. There is no reason, however, why this should be so.

I have recently had the exceptional opportunity of directing treatment for a long period in a patient who had a severe hemiplegic attack, and, although it is now over a year since the stroke, there is not the slightest suspicion of contracture. Ordinarily, marked contractures would have been apparent by this time. The following treatment was carried out, starting two months after the attack:

General massage was applied morning and evening, but particular attention was paid to the muscles which were known to be more paretic; *i. e.*, in the upper limbs the extensor and in the lower the flexor muscles. Every other day faradic electricity was applied, but especially as in massage to the weaker muscles.

As the return of power became apparent splints were applied both to the upper and lower limbs. A straight palmar splint extending from the elbow to the finger-tips and a felt posterior foot and leg splint were used, so as to keep the hand and fingers and the foot in the normal position. These were always applied at night when the patient went to bed, as no difficulty was experienced while the patient was awake.

Forced movements were practised twice daily, these being mostly such as could be least performed, as, for instance, elevation of the shoulder; extension of the elbow, wrist, and fingers; flexion and abduction of the thigh and foot. These were not carried on sufficiently to tire the patient, and they were prolonged gradually. As the patient began to walk a shoe was so constructed as to naturally keep the foot in its normal position.

Instead of faradic, galvanic electricity may be used, but here the object would be to relax the stronger muscles, and therefore the current should be so applied. This is useful, but perhaps not so much so as the faradic application.

Acting on the theory that certain muscle groups have a better return of function in hemiplegia than others, Spiller[28] recently recommended an operation of nerve anastomosis, to strengthen the weaker muscle groups. Thus, in the hand, the flexors being stronger than the extensors, he proposed anastomosing the central ends of the flexor nerves to the peripheral ends of the extensor nerves. In one unfavorable case in which this was done, by Frazier, in a woman of sixty-five, the results were not fully encouraging. There is every reason to believe, however, that this method should give good results, for in another case of athetosis in a cerebral diplegic brilliant results were obtained. Partial failure in the first case is probably due to the age of the patient, the imperfect return of power before the operation, and the length of time that elapsed between the stroke and the operation, five years. It is probable that such an operation performed within a year of a hemiplegic attack would give better results.

Oppenheim[29] has very recently cautioned against tendon transplantation for the return of function in paralyzed muscles in which the symptoms are progressive. Spiller justly remarks that, where applicable, nerve anastomosis or nerve transplantation is to be preferred to tendon transplantation because the latter makes no demand upon the paralyzed muscles.

So far as the contractures due to disease of the pyramidal tracts are concerned, they can to a large extent be avoided by judicious massage, electricity, and mechanical methods similar to those employed in hemiplegia.

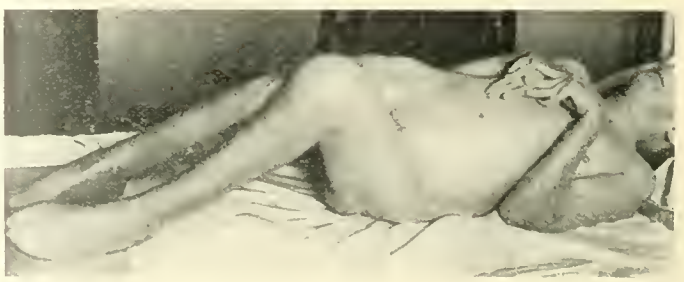

Fig. 4.—Paralysis agitans with contractures resembling those of arthritis deformans.

In anterior poliomyelitis, the contracture being passive, proper mechanical appliances which prevent overaction of the non-paralyzed muscles may prevent contracture. Galvanic currents applied to the paralyzed muscles are of great value. Both tendon transplantation and nerve anastomosis have been employed and are of use in judiciously selected cases, where the paralysis is limited to a few muscles. In a case operated upon by J. K. Young at Dr. Spiller's suggestion, in which the anterior tibial muscle alone was diseased, anastomosis of the branches of the anterior tibial to the musculocutaneous nerve gave brilliant results.

Many of the contractures present in this disease, as well as in multiple neuritis and in neuritis of one nerve, are the result of faulty positions. Thus, in a musculospiral or peroneal palsy, unless the hand or the foot is properly supported, structural changes will result, with marked contractures. Precautions should always be taken to keep these parts in their normal positions by the application of splints.

Bibliography.

1. Todd. Clin. Lect. on Paralysis, etc., London, 1856.
2. Gowers. Diseases of the Nervous System, p. 82.
3. Von Monakow. Gehirnpathologie, 1897, p. 311.
4. Duchenne. Phys. der Bewegungen, Uebers. v. Wernicke, 1885.
5. Spiller. American Journal of the Medical Sciences, July, 1902.
6. Brissaud. Recherches sur la contr. des hemipleg., Paris, 1880.
7. Dignat. Le progrès méd., 1883, vol. ii. p. 802.
8. Spiller. Univ. of Penna. Med. Bulletin, Jan., 1905.
9. Bouchard. Arch. gén. de méd, 1866, vol. i. and ii.
10. Charcot. Arch. de physiol. norm. et pathol., 1868.
11. Hitzig. Quoted by von Monakow.
12. Mann. Zeitsch. f. diät. u. physikal. Behandlung, vol. vi. p. 115.
13. Lazarus Ibid.
14. Van Gehuchten. Quoted by Rothmann.
15. Von Monakow. Gehirnpathologie, 1897, p. 316.
16. Oppenheim. Lehrbuch der Nervenkr., 1905, p. 696.
17. Rothmann. Berlin. klin. Wochensch., 1902. No. 17 and 18; Zeitshr. f. klin. Med., vol. xlviii. p 10; Deutsch. med. Wochen., 1903, No. 24 and 25.
18. Parhon and Goldstein. Roumaine Med., 1899, No. 2.
19. Marinesco. Semaine méd., Nov. 23, 1898.
20. Weisenburg. Journ of the American Medical Association, Feb. 25, 1905.
21. Alban and Infe'd. Obersteiner's Arbeiten, 1902, vol. ix.
22. Von Bechterew. Deutsch. Zeitshr. f. Nervenkr., 1900.
23. Spiller. Philadelphia Medical Journal, 1899.
24. McCarthy. American Journal of the Medical Sciences, 1902.
25. Pfeiffer. Neurolog. Centralbl., 1901.
26. Spiller. Univ. of Penna. Med. Bulletin, May, 1904.
27. McCarthy. New York Medical Journal, May, 1905.
28. Spiller and Frazier. Journal of Nervous and Mental Disease, May, 1905.
29. Oppenheim. Berliner klin. Wochenschrift, 1905.

THE DIFFICULTY OF DIAGNOSTICATING BETWEEN TABES AND CEREBROSPINAL SYPHILIS, WITH A REPORT OF TWO ILLUSTRATIVE CASES.

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The tabes-syphilis question has been a fruitful topic of discussion for a long period of time, but most regard seems to have been paid to the etiological relation and but little to the differential diagnosis. That this diagnosis may be extremely difficult, the two cases that I have to report in this paper very well illustrate.

These cases were in the service of Dr. William G. Spiller at the Philadelphia General Hospital, to whom I am indebted for the clinical notes and the pathological material.

A. M., a white man, aged fifty-two years, by occupation a carpenter, complained on admission of inability to walk in the dark and of a loss of muscular control in his limbs, accompanied by wasting of the muscles. His family history was negative. His father died as the result of an abscess of the ear, and his mother from some cause unknown when the patient was only ten months old. One brother died of alcoholism, one brother and one sister died of pneumonia, and one sister died of scarlet fever. There was no family history of pulmonary, cardiac, kidney, or neoplastic disease. The patient had measles, whooping-cough, and scarlet fever when a child. He had gonorrhœa once, and a chancre about thirty-two years ago.

He used alcohol and tobacco moderately. He has been married thirty years, and his wife has locomotor ataxia. From this union there were nine children, six of whom died in infancy of unknown cause and three died of diphtheria.

The patient said that his present illness began twenty-three years ago with a "neuralgia" in his head, which has since that time "gone down to his legs," and he has had "rheumatic pains" in them. About ten years ago he noticed that when he closed his eyes he staggered, and that he could not walk in the dark. He had a girdle sensation about his waist. He has been very constipated, having to take laxatives constantly, and he has had difficulty also in passing his urine, but at night it would dribble from him. He had vertigo at times and difficulty in holding an article in his hands.

On admission, February 16, 1904, it was noted that his pupils were equal and the extraocular muscles normal. The right pupil reacted in accommodation, but the left did not. Neither pupil reacted to light. The tongue was tremulous and coated, but was protruded in the median line and was not atrophied. The pulse was slow, but of fair volume. His body was poorly nourished. The chest large, with the costal angle obtuse. There was a groove on each side of the chest at the level of the seventh rib.

The muscles of the hands, arms, legs, and feet were much wasted. The arms were ataxic and the gait markedly so; he could not walk or stand unsupported. The biceps-jerks and knee-jerks were lost on each side, even on reinforcement. He could not determine the size or shape of objects placed in his hands.

Notes made October 19, 1904, are as follows:

The limbs are very stiff and weak. Both legs and arms are spastic. The reflexes are lost. Both pupils react to light and accommodation, and the extraocular muscles are normal.

There is no facial palsy. He complains of pain in the cervical region of the spine. He has a coarse tremor of both hands and the hands are wasted, but he says that they are better now than when he was admitted to the hospital. He has complained of deafness and tinnitus for the past three days. His treatment has been mercury and iodide of potash.

For two weeks previous to his death he had recurrent attacks of severe pain in the stomach, associated with vomiting, supposed to be gastric crises. He was apparently recovering, when, on November 10, 1904, he suddenly died.

At an autopsy held the next day it was found that death was due to acute dilatation of the heart. There was a chronic emphysema of the lungs, but the other organs were apparently normal. The brain and spinal cord were removed and showed no gross pathological changes. A histological examination reveals the following facts:

The pia-arachnoid over the paracentral lobules shows a considerable degree of round-cell infiltration. Numerous corpora amylacia are found in the outer part of the cortex. Some of the Betz cells show marked alteration, such as peripheral displacement of the nucleus and chromatolysis, but most of them are in a fairly normal condition. There is extensive round-cell infiltration in the pia surrounding the optic chiasm and nerves, and also about the bloodvessels within the chiasm, but, with the exception of one small bundle of nerve fibres about the middle of the nerve, there is no degeneration by the Weigert hæmatoxylin method.

The round-cell infiltration and vascular congestion in the pia of the medulla oblongata is intense, and some perivascular round-cell infiltration is also seen within the medulla oblongata. The anterior pyramids, by the Weigert method, are not degenerated.

In sections from the upper cervical region the posterior columns and posterior portions of the lateral columns are much degenerated, and the round-cell infiltration of the pia and about the bloodvessels within the cord is intense. The extramedullary bloodvessels are greatly thickened. At one place a distinct mass of round cells extends from the pia into the cord, forming a small gumma. At the beginning of the cervical swelling the posterior columns are still much degenerated, and there is considerable degeneration of the periphery of the cord, especially in the right anterolateral column. A little lower the degeneration in the anterolateral column is not so marked.

In the thoracic region the degeneration is very pronounced in the posterior columns and in the periphery of the anterolateral columns, but it is not so marked as in the upper cervical region. This degeneration is much the same in sections from all levels of this region.

In the lumbosacral region the posterior columns are much degenerated, and throughout the whole spinal cord the degeneration resembles very closely that of tabes. There is also some degeneration of the anterolateral columns. On the thoracic and lumbar regions the pia is thickened and infiltrated with round cells.

Sections from the lumbar region stained by the thionin method show very marked degeneration in the nerve cells of the anterior horns, consisting of marked chromatolysis, with displacement of the nucleus, vacuolation, swelling, and loss of dendritic processes.

To summarize, we have, clinically, a man who, thirty-two years previously, contracted syphilis, and presenting on admission Westphal's symptom, Romberg's symptom, Argyll-Robertson pupils, ataxia of arms and legs, girdle sensation, pains in the legs, and urinary disturbances. Eight months later it is noted that the arms and legs are spastic, although the reflexes remain lost, and that the Argyll-Robertson pupillary reaction had become normal. The hands, arms, legs, and feet were wasted. After his death a histological examination revealed a degeneration in the posterior columns throughout the length of the spinal cord, the typical lesion of tabes dorsalis. It was only by other lesions, the round-cell infiltration of the pia and about the bloodvessels, and the characteristic thickening of the bloodvessel walls that the real nature of the affection could be diagnosed pathologically.

The second case I have to report is: T. L., aged forty-seven years, whose chief complaint was difficulty in walking. His family and previous medical histories were negative.

About three years before admission he began to have an aching in the calves of his legs, which persisted intermittently. One year later he had an attack of sudden unconsciousness, only lasting a minute, but which kept him in bed for seven weeks following. Since that time he has had a more or less constant headache, and his vision was dimmed. He said that he had had diplopia, and that his legs felt numb. He walked with great difficulty.

Examination by Dr. Spiller: Atrophy in the lower limbs is very marked, but power is retained in all the muscles, although diminished. The knee-jerks are entirely abolished on each side, even on reinforcement. The Achilles jerks are lost on each side. The plantar cutaneous reflex of either side is exaggerated. Tactile sense is preserved everywhere, and pin-prick is sharply felt. The motive power of the upper limbs is fairly good, and the upper limbs are not atrophied, although the tonicity of the muscles is diminished. Voluntary motion of the upper limb causes a fine tremor throughout the limb. The pupils are unequal, the right being smaller than the left, but they are regular in outline. The irides contract to light, but the action is exceedingly slow, whereas the contraction in accommodation is very prompt. He is able to stand with his feet wide apart, but his station is very uncertain. He can take a few steps, if well supported,

but he is in great danger of falling. He has had incontinence of urine and feces for about one month past.

At autopsy there were no gross pathological lesions in the brain or spinal cord, but a histological examination reveals the following conditions:

There is intense round-cell infiltration in the pia and about the bloodvessels in the paracentral lobules. The bloodvessels of the pia and of the cortex are congested, and their walls are much thickened. The Betz cells appear to be normal. There is intense round-cell infiltration of the pia and about the bloodvessels at all levels of the spinal cord, and there is a border zone of degeneration in the cord in all the sections.

Sections from the medulla oblongata stained by the Weigert method appear to be almost normal, but stained by a nuclear method show a round-cell infiltration of moderate degree about the bloodvessels within the medulla oblongata, and an intense round-cell infiltration of the surrounding pia. A few small holes are found in the anterior pyramids of the medulla oblongata where nerve fibres have disappeared. Sections of the optic chiasm show intense round-cell infiltration of the pia and also about the bloodvessels within the chiasm, and the bloodvessels are thickened.

There is degeneration of the posterior columns in the cervical and thoracic regions, and to a slight extent in the lumbar region. The crossed pyramidal tracts are not degenerated in the cervical or midthoracic region, but there is moderate degeneration in each crossed pyramidal tract in the lumbar region. The posterior roots in the lumbar region are infiltrated with round cells, and their bloodvessels are much thickened and congested. They contain a number of swollen axis cylinders and numerous spaces from which fibres have disappeared. It is impossible to study the condition of the nerve cells of the anterior horns of the spinal cord by the thionin method, as the material was hardened in Müller's fluid.

To summarize this case: Clinically, the patient presented ataxia of the lower limbs, combined with pain, atrophy, and loss of reflexes. He had incontinence of urine and feces, with a marked slowing of the iridic response to light, while it remained prompt in accommodation. Pathologically, there was found a degeneration of the posterior columns like that of tabes, combined with the characteristic lesions of cerebrospinal syphilis.

Cases of syphilitic pseudotabes have been reported by Oppenheim, Eisenlohr, Siemerling, Brasch, Ewald, Valentin, and others, and beyond doubt there are many such cases that are regarded as cases of tabes.

Oppenheim (quoted by Nonne) said in a discussion of Valentin's case before the Berliner Gesellschaft für Psychiatrie und Nervenkrankheiten, December 12, 1898, that many cases of juvenile tabes in the literature described as due to hereditary syphilis were in reality cases of syphilitic pseudotabes. From a pathological standpoint, it can easily be seen how the syphilitic pseudotabes may be mistaken for true tabes. The degeneration of the posterior columns of the cord in cases of tabes is ascending and due to a degeneration of the posterior roots extending from the posterior root ganglia. Exactly the same degeneration would be produced if the posterior roots were compressed to the point of destruction by the thickened meninges. However, the usual degeneration of the cord in cases of syphilitic meningitis, the annular degeneration, is caused by interference with the centripetal blood supply which comes from the posterior spinal arteries. The nourishment of the posterior columns is almost entirely by this centripetal system of arteries, which are not only of larger calibre here than in the anterolateral divisions of the cord, but penetrate much more deeply.

The white matter of the anterolateral columns is supplied to some extent by arteries from the centrifugal blood supply, extending outward from the gray matter. On account of this peculiar distribution of the blood, any interference with the centripetal system such as would occur in syphilitic meningitis would cause a much more marked degeneration in the posterior columns than in the anterolateral columns, which would probably also be of earlier onset. This latter statement is borne out by the histories of these cases. In the earlier stages they are indistinguishable from cases of true tabes; later on a certain amount of spasticity due to involvement of the lateral columns might lead to the correct diagnosis.

There is another aspect of the subject which perhaps deserves consideration, and that is whether these cases might not be regarded as examples of tabes and syphilis combined. It has always been a weak point in the argument that syphilis is the cause of tabes, that so few cases of tabes show any pathological evidence of the presence of syphilis. Attention is called to this fact by Nonne, who refers only to the papers of Hoffman, Sidney Kuh, Schwarz, Cassirer and Strauss, Dejerine, and Dinkler as reporting cases of tabes combined with syphilitic lesions, either in the nervous system or elsewhere in the body.

The diagnosis between tabes and syphilitic pseudotabes is difficult to make pathologically, and is even more difficult clinically.

Nonne well says that "there is no pathognomonic symptom of spinal syphilis." The same may be said of tabes, and there is no symptom or set of symptoms that will serve at one examination to distinguish positively between them.

Considering, seriatim, the diagnostic symptoms of each, it appears that a history of previous specific infections is as frequent in one as in the other, although statistics on this point would show a wide difference of opinion, as there is a difference of opinion as to the number of cases of tabes giving a history of previous specific infection.

From a study of the literature it would seem that a total loss of the pupillary reflexes is more common in syphilitic pseudotabes than only a loss of the reflex to light, but in both of my cases there was certainly a greater loss of the reflex to light than of the accommodation reaction, and, on the other hand, I have seen several cases of syphilitic meningomyelitis with typical Argyll-Robertson pupils.

Inequality of the pupils or irregularities in their outline would point to syphilis, as would possibly also any extra-ocular palsies, although the latter are common in tabes. The optic nerve would more likely show a neuritis than a primary atrophy if the change were due to active syphilis.

Other signs—lost knee-jerks and lost Achilles jerks, ataxia, and Romberg's sign—are certainly more frequent in tabes, but their occurrence in cases of spinal syphilis must always be recognized. As these cases of pseudotabes syphilitica progress, there is often noted some spasticity of the limbs, caused by the later involvement of the lateral tracts in the degeneration. This spasticity is not seen in cases of genuine tabes, and would enable the diagnosis to be made; however, it is then too late for specific treatment to be of as great benefit as at an earlier period of the disease. The importance of making the correct clinical diagnosis in as early a stage as possible is very evident. True tabes is usually regarded as incurable, and any treatment so far proposed has been unsatisfactory; on the contrary, the treatment of syphilis of the nervous system by the exhibition of antisyphilitic remedies has sometimes given surprisingly good results, especially in the earlier stages of the disease. It would seem that with the great difficulty in diagnosticating between tabes and syphilitic pseudotabes, it would be a wise measure, in any case where tabes is suspected, to give a thorough treatment with antisyphilitic drugs.

The first case, A. M., affords a confirmation of a conclusion at which I arrived in a study of muscular atrophy in tabes, published in the University of Pennsylvania Medical Bulletin, January, 1905, namely, that changes in the anterior-horn cells are the cause of the atrophy. In this case muscular wasting was a prominent feature, and one of the patient's chief complaints on admission to the hospital. On histological examination by the thionin stain, it was found that the anterior-horn cells were intensely diseased.

References.

Brasch. Deut Zeit. f. Nervenheilk, 1901, vol. xx.

Cassirer and Strauss. Monat für Psych. und Neurolog., 1901, Bd. x., H. 4.

Dejerine. Arch. de phys. Norm. et Pathol., 1884.

Dinkler. Deut. Zeit. für Nervenheilk., 1893, Bd. iii.

Eisenlohr. Westphal's Archiv, Bd. xxiii.

Ewald. Berl. klin. Wochenschr., 1893, No. 12.

Hoffman. Sitzung der Naturhist. Verein zu Heidelberg, July 1, 1890 (reference given by Nonne, l. c.).

Kuh. Westphal's Archiv, 1891, Bd. xxii.

Nonne. Syphilis und Nervensystem, Berlin, 1902. Berliner klin. Wochenschr., 1899, No. 15.

Schwarz. Zeit. f. Heilkunde, 1897, Bd. xviii.

ON THE EFFECT OF INTRAPERITONEAL INJECTIONS OF LEECH EXTRACT ON THE COAGULATION OF EXUDATE.

A Preliminary Note.

By Leo Loeb, M.D.,

Assistant Professor of Experimental Pathology, University of Pennsylvania.

As pointed out in some former papers,[1] an analysis of the factors underlying coagulative processes is not only of significance for an understanding of the changes taking place in the blood after it has left the body and inside the blood-vessels in thrombosis, but it is also necessary for an understanding of certain inflammatory processes, as, for instance, the formation of fibrinous exudate.

The pathological significance of the solidification of peritoneal exudate is mainly due to the fact that connective-tissue cells and bloodvessels, which do not usually grow into liquids, begin under certain conditions to advance into solid coagula. This organization of a coagulum by connective tissue transforms the fibrinous into a fibrous adhesion.

In the course of a study of the formation of fibrinous exudate, I carried out a few experiments on the effect of intraperitoneal injections of hirudin under conditions which usually cause either localized or more general fibrinous adhesions.

For the production of localized adhesions guinea-pigs were used. Pieces of agar were introduced into the peritoneal cavity. In some animals plain agar was used; in others agar which had been previously soaked in a 2 per cent. watery solution of iodine, to which 4 per cent. of sodium iodide had been added; pieces of agar soaked in 95 per cent. alcohol were also employed. The peritoneal wound was closed and

[1] Montreal Medical Journal, July, 1903; Virchow's Archiv, 1904, vol. clxxvi.

leech extract was injected immediately afterward. A 0.6 per cent. solution of hirudin in a 0.85 per cent. NaCl solution was used. The injection was repeated in certain intervals and different quantities of hirudin were injected in different animals. Control guinea-pigs received the same number of injections of a 0.85 per cent. NaCl solution to which thymol had been added, the preparation of leech extract containing likewise thymol. The animals were killed eleven, twenty-four, and twenty-eight hours after the introduction of the agar.

The difference between the guinea-pigs treated with injections of hirudin and those receiving injections of a sodium chloride solution with thymol was quite marked. In the former the large majority of the pieces of agar were lying free in the abdominal cavity and only a few were in some animals slightly fixed to the large omentum.

The majority of the pieces in the control guinea-pigs, on the other hand, were more or less firmly fixed to the omentum, liver, intestines, and mesentery; some of the pieces were lying free at the parietal peritoneum.

From these experiments we may conclude: (1) that repeated injections of leech extract diminish considerably the coagulation of localized exudate and the formation of localized fibrinous adhesions; (2) that it has not yet been possible to avoid the formation of adhesions altogether, although relatively large doses of hirudin were injected; and (3) that under these conditions the large omentum is especially prone to fix to itself foreign particles by adhesions.

Whether the adhesions found at the large omentum are due to the formation of a slight fibrinous exudate or whether they are due to cell changes has still to be investigated. The method indicated promises to decide with certainty whether adhesions do occur without the intervention of fibrin. Such adhesions have been described by Graser.

For the production of adhesions extending over large areas, rabbits were injected with a 2 per cent. of iodine in a 4 per cent. sodium iodide solution. These latter experiments are not yet concluded, and a more detailed report shall be given later. So far the results obtained point to the conclusion that it will probably be possible to reduce at least temporarily the number and extent of fibrinous adhesions in rabbits and guinea-pigs by the repeated injections of leech extract.

BOOK REVIEWS.

THE OPHTHALMIC YEAR BOOK: A DIGEST OF THE LITERATURE OF OPHTHALMOLOGY, WITH INDEX OF PUBLICATIONS FOR THE YEAR 1903. By EDWARD JACKSON, A.M., M.D., Emeritus Professor of the Diseases of the Eye in the Philadelphia Polyclinic; President of the American Academy of Ophthalmology and Otolaryngology; Ophthalmologist to the Denver County Hospital, St. Anthony's Hospital, and Mercy Hospital, Denver, etc. Denver: Herrick Book and Stationery Co., 1904.

All books giving condensed accounts of the literature of the world are welcome books to the general practitioner; and this is especially true of the subject of "Ophthalmology," as so much of value is written in languages foreign to the average practitioner or even specialist. Many ophthalmic journals contain abstract departments for this very reason, but systematic arrangement is only possible in a book appearing yearly. This book gives a critical digest, as stated by the author in his announcement, of the most important literature, judging it from the standpoint of the ophthalmic surgeon. It also gives a list of the more important original communications appearing during the year. The book is recommended warmly to every reader of medical literature. E. L.

MEDICAL LABORATORY METHODS AND TESTS. By HERBERT FRENCH, M.A., M.D. (Oxon.), M.R.C.P. (Lond.), Medical Registrar, Guy's Hospital Gillson Scholar, Society of Apothecaries of London; Radcliffe Travelling Fellow, Oxford University. Chicago: W. T. Keener & Co., 1904.

This is a small volume of 152 pages, giving in a condensed and practical form the chemical and microscopic tests and investigations most useful to medical men. It does not pretend to contain all the methods, but only those employed most commonly; their advantage and fallacies are both related. Bedside examinations of patients are not touched upon at all. The section on the urine is especially complete and will be found very useful. The section on the blood, if carefully read, will show the general practitioner how easily the tests for the study of this fluid may be performed, and the same may be said of most all of the other chapters. The chapter on feces, considering the importance of the subject to the practitioner, is lamentably short. The index is complete and the tests can be easily found. We can cordially recommend the book as useful to busy practitioners.

E. L.

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DEPARTMENT OF MEDICINE

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This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

A STUDY OF METABOLISM IN LEUKÆMIA, UNDER THE INFLUENCE OF THE X-RAY.

With a Consideration of the Manner of Action of the X-ray and of Some Precautions Desirable in its Therapeutic Use.[1]

By John H. Musser, M.D.,
Professor of Clinical Medicine, University of Pennsylvania,

and

David L. Edsall, M.D.,
Assistant Professor of Medicine, University of Pennsylvania.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

Recent observations and experiments have furnished most impressive testimony of the power of the *x*-rays for both good and evil, and the most remarkable of the favorable influences that have been observed in the past two years is that exerted upon leukæmia. Indeed, in the extent of the tissue changes induced the effect in leukæmia more than equals that seen in any other disease. It is true, to be sure, that, as is so commonly the case in cancer, the benign effect upon leukæmia is only temporary, most of the cases in which apparent recovery occurred having relapsed, and none of them having as yet provided any evidence that relapse can be avoided. Nevertheless, numerous cases of leukæmia have now been observed in which complete, or almost complete, temporary disappearance of symptoms was seen as a result of *x*-ray treatment, and an equal degree of success with other forms of treatment is rare to an extreme.

On the other hand, the evil effects of *x*-rays have attained recently a disquieting degree of prominence. For some time past occasional instances have been recognized in which, in leukæmia and in other diseases, exposure to *x*-rays produced more or less severe, and sometimes even dangerous, febrile reaction, chills, vomiting, prostration, and other pronounced general symptoms that had the appearance of being caused by an intoxication. We have also lately learned that occasionally serious lesions, such as nephritis, have followed the use of *x*-rays, and an astonishing and deplorable effect upon the reproductive function has been demonstrated by the work of Albers-Schönberg and others. Furthermore, Heineke, Warthin, and others have described rapid and widespread changes in the tissues after the use of *x*-rays; the alterations in the lymph glands and bone-marrow found by Heineke in his extensive experiments being extremely startling and impressive.

It has, therefore, become plainly evident that, in addition to the "burns" that have long given occasion for caution in the use of *x*-rays, there are other unfortunate effects that may be more rapid in their appearance and that are at times much more grave. It is not surprising that an agent that is capable of producing profoundly benign effects should also have the power of doing great harm unless used with full knowledge of the manner in which its effects are brought about, and this has not been the case with *x*-rays. The indications for employing them and the dangers associated with their use have been determined chiefly by empirical means, while the nature of their action has remained a mystery.

Our investigations of the changes in metabolism that follow *x*-ray treatment of leukæmia have demonstrated in a striking manner that the influence upon metabolic processes is extremely rapid and very profound, and our results emphasize most forcibly the possibilities in *x*-rays for the production of both good and bad results. They indicate also, we believe, with considerable clearness the general way in which *x*-rays act.

The effect upon metabolism that we observed is probably unequalled by that known to be due to any other therapeutic agent. Radium is probably capable of equally marked effects, but it has not been studied in a similar way. Other therapeutic agents may, to be sure, have profound results when they are used in doses that largely exceed the therapeutic limit; but such results are definitely toxic, not therapeutic. With the *x*-ray, on the contrary, our observations appear to indicate clearly that tissue destruction is, in leukæmia, evidence of favorable action, while when the *x*-ray fails to act this tissue break-down does not occur. This is a most striking fact, and one that is quite the reverse of the usual conditions. Rapid break-down of body tissue is, of course, ordinarily extremely harmful, especially when protein tissue is being destroyed; in one of our leukæmics, how-

[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May 16 and 17, 1905.

ever, we observed the interesting phenomenon of rapid symptomatic improvement, occurring coincidently with tremendous acceleration of protein tissue destruction, while in the other leukæmic, whose disease was progressing toward a fatality, the *x*-ray exerted extremely little influence upon metabolism, the destruction of tissue was scarcely at all excessive, and, as death approached, tissue break-down not only did not increase, but appeared to grow progressively less. The changes that have been seen clinically and at autopsy in the condition of the spleen, the lymph glands, and the blood, in cases of leukæmia that have improved under this treatment, and particularly the remarkable experimental work of Heineke, appear to show that the tissue destruction produced by the *x*-ray is limited largely to the lymphatic tissues and the bone-marrow; Heineke, indeed, could find no changes in other tissues. Hence the fact that symptomatic improvement occurs in leukæmia while tissues are undergoing rapid destruction seems to be the result of the limitation of this tissue disintegration, chiefly, or possibly entirely, to the diseased parts.

Rather than lessening its importance, this apparent limitation of the effects to certain tissues adds to the interest of the subject in its relation to general metabolism.

Our studies of the behavior of metabolism in leukæmia while *x*-ray treatment was being used were, as we have already indicated, carried out in two cases. We wish particularly to emphasize the contrast between these two cases, for the opportunity to compare the conditions during successful treatment with those during unsuccessful treatment led to what is, perhaps, the most suggestive result of the study. One case had previously been subjected to this treatment with success, and nearly all symptoms had then disappeared, but they returned, and when our observations on metabolism were made the symptoms were growing worse continuously, in spite of the use of *x*-rays, and the patient soon died. In the other case, on the contrary, severe symptoms were present when *x*-ray treatment was instituted, and the patient was growing worse at that time, but the use of *x*-rays resulted in immediate and very rapid improvement, and the patient left the hospital a few weeks later, showing only slight evidences of leukæmia.

The influence of *x*-rays upon metabolism was studied also in two cases of severe gout (by Dr. Edsall and Dr. Fife), and in another case (Dr. Edsall), in which the conditions of metabolism were practically normal. The details of these cases will be published elsewhere, but the results will be referred to in this paper, in so far as they bear upon the conclusion to be reached concerning the way in which the *x*-ray acts.

Both leukæmies were private patients of Dr. Musser. Both were told that *x*-ray treatment of leukæmia is still somewhat of an experiment, and that there is an element of danger in it, but both wished the treatment to be tried. It was impossible to subject them to rigid limitation of the diet for a long time. Both had poor appetites, particularly the first patient, and they soon rebelled against the monotonous diet; consequently the period of study was brief, and some minor details (such, for example, as the duration of the effect of the *x*-ray) that could be determined only by more prolonged study were necessarily left unsettled. The main points sought for were, however, made sufficiently clear by the results that were secured. The figures obtained in both cases in the study of metabolism will, for the sake of contrast, be put together, following the clinical synopsis of the two cases.

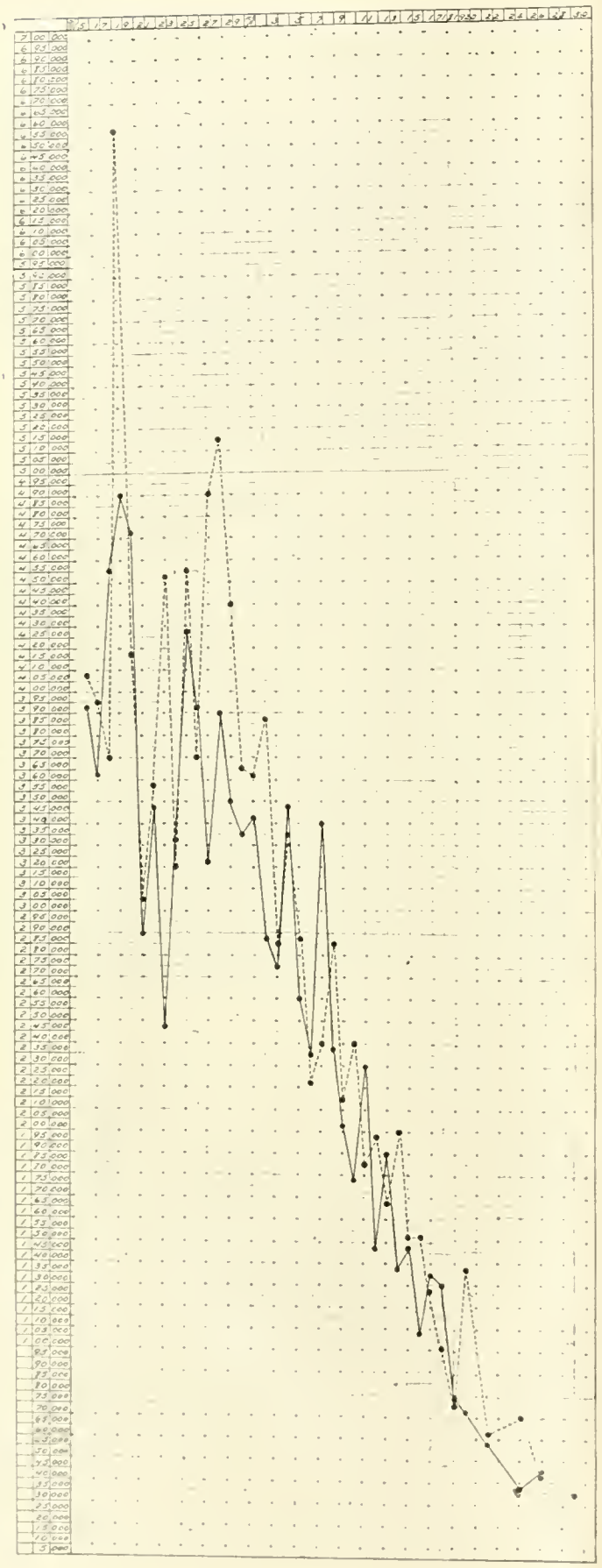
Only the main clinical details will be given.

Case 1.—The fatal case. The patient, E. C. H., a man aged forty-four years, a plumber, was first admitted September 15, 1904, to the private wards of the University Hospital. He had no family or personal history that was of any noteworthy consequence until March, 1904, when he began gradually to lose strength; the weakness had increased from this time, but he had noticed no other symptoms, except mental irritability and occasional attacks of diarrhœa. At the time of admission he showed the conditions usual in a marked splenomyelogenous leukæmia. The spleen then extended from the seventh rib in the anterior axillary line to three inches below the level of the umbilicus, and anteriorly nearly to the median line, its greatest length being twelve and one-half inches, its greatest breadth thirteen inches. The liver was not enlarged; the inguinal and axillary glands were palpable, but not of large size. The blood examination showed hæmoglobin, 38 per cent.; red blood cells, 4,280,000; white blood cells, 407,500. A differential count made on the 21st showed:

Myelocytes	49.2 per cent.
Polymorphonuclears	27.1 "
Transitionals	21.6 "
Eosinophiles	1.0 "
Lymphocytes	0.2 "

There were also 0.8 per cent. of nucleated reds. The patient was at once put upon *x*-ray treatment and very rapidly improved, the behavior of his leukocytes being shown by the accompanying chart that was made by the resident physician, Dr. Thomas Kelly. The continuous line indicates the counts before the *x*-ray treatments; the broken line the counts taken directly after the *x*-ray treatments.

At the time of discharge, on October 13th, the leukocyte count was 138,000; the spleen had decreased greatly in size, and the patient's general condition was very much improved. The leukocytes subsequently fell to below 35,000, and the spleen became about normal in size. He left because of the demands of his business, but had *x*-ray treatments at first daily, afterward once or twice a week, until February, 1905. He then stopped coming for treatment. He was readmitted



Leukocyte counts made before and after *x*-ray exposures from September 15, 1904, to October 30, 1904. The unbroken line (———) indicates counts before exposure to *x*-rays, the broken line (– – –) the counts after exposure.

on March 12, 1905, having rapidly grown much worse, and having recently had pain and soreness in the muscles, with fever and considerable weakness, and with renewed enlargement of the spleen. Upon examination his spleen was found to reach the level of the umbilicus, and the leukocyte count was 180,400.

The differential count (Dr. A. O. J. Kelly) showed:

Basophiles	4.0 per cent.
Lymphocytes	4.0 "
Polymorphonuclears	18.0 "
Eosinophilic myelocytes	2.5 "
Neutrophilic myelocytes	71.5 "

Several nucleated reds were seen. The man had slight fever, which continued afterward, running as high as 101°. He grew rapidly worse, and on the 21st, the day that the observation of metabolism was started, his leukocyte count was 304,000. Because of his bad condition the preliminary observation of metabolism was continued but two days, and on the 23d *x*-ray treatment was started. For several days after this he seemed to feel better, though there was no improvement in the leukocytes; on the contrary, they grew continuously more numerous, the count being 453,600 on the 26th; 496,000 on the 29th. He also developed fresh hemorrhages into the retina. Suddenly, on the 31st, he went into temporary collapse; the following day he was very weak, and early the next morning he again went into collapse and died. A postmortem could not be secured.

Case II.—The successful case. The patient, Mrs. L., aged forty-two years, was admitted to the private wards of the University Hospital on March 20, 1905. Her history previous to October, 1903, was without interest. At that time she became easily fatigued, lost flesh, and her color rapidly changed and became "greenish." She also noted enlargement in the splenic region. After general treatment she improved very greatly, and by the spring of 1904 had, she believed, regained her normal health. This continued until October, 1904, when she had a slight operation for a cyst of the eyelid, and hemorrhage continued for nine hours from the small incision. She lost a great deal of blood and was much shocked afterward, and her spleen almost at once became enlarged, while her general condition grew gradually worse up to the time that she was admitted. When seen by Dr. Musser she presented marked features of leukæmia, the spleen extending from the seventh interspace in the anterior axillary line to within an inch of Poupart's ligament, and anteriorly it reached beyond the median line. The liver was not enlarged; there was no marked glandular enlargement. The blood count showed 68 per cent. hæmoglobin; 3,410,000 red blood cells; 245,000 white blood cells.

The differential count (Dr. A. O. J. Kelly) showed:

Neutrophilic myelocytes	45.0 per cent.
Basophilic myelocytes	16.0 "
Eosinophilic myelocytes	3.0 "
Polymorphonuclears	26.0 "
Lymphocytes	9.0 "

The patient was weak and very pallid, and appeared emaciated. She felt worse during the next few days, and on the 23d, when the metabolism experiment was started, the leukocyte count was 272,000; on the 26th, when *x*-ray treatment was begun, it was 304,400. Directly after this continuous improvement began, and the spleen decreased rapidly in size, so that on April 20th, when she was discharged, the lower border was but slightly below the umbilicus, and the anterior border was fully two inches within the median line.

The leukocyte counts had been as follows: March 27th, 262,400; 28th, 252,400; 29th, 246,400; 30th, 214,400; 31st, 191,200; April 1st, 149,600; 4th, 96,000; 5th, 80,080; 7th, 40,080; 9th, 32,800; 11th, 30,400; 13th, 24,720; 15th, 28,440; 17th, 17,440; 18th, 15,200; 20th, 15,360. She returned for blood counts and *x*-ray treatment until May 8th. During this time the counts were: April 26, 12,480; 30th, 6480; May 8th, 9040.

For the study of metabolism both patients were put upon a diet of milk, bread, butter, eggs, sugar, rice, steak, baked potato. The amount taken each day was kept as nearly the same as possible, and the quantity actually taken was accurately weighed each day; it was not possible with either patient to make the daily intake absolutely uniform, but the variations were slight and not important.

The amount of nitrogen and P_2O_5 in the food in each case was calculated partly from a large series of analyses that we had previously made of the same foods as they are used in the University Hospital, partly from the figures of König and Blythe, chiefly from our own figures. The nitrogen, P_2O_5, uric acid (Folin-Schaeffer method), and purin bases (Salkowski method) of the urine were estimated daily. The feces for each period were collected as a whole, dried, ground, and the nitrogen and P_2O_5 contained in them estimated in a number of different portions. The total amount in the feces was determined from the average of these estimations. In both cases the diet was given for three days before the metabolism experiment was begun. In both instances there was then a preliminary control period of observation of metabolism, which was made very short in each instance, because both patients were so ill that it seemed unjust to delay the use of *x*-rays for a longer time; this period was two days in length in the first case, three days in the second. There was then a period of observation, three days long in both cases, during the use of *x*-rays. After this it was necessary to relinquish the rigid diet, since both patients refused to take it longer. Consequently the intake could no longer be accurately determined, but for some time afterward the nitrogen, P_2O_5, and uric acid of the urine were determined in each case, and the figures obtained, which provide some interesting observations, will be given in separate tables, following those that exhibit the metabolic balance.

TABLE I. CASE 1. PRELIMINARY PERIOD.

Date.	Urine.				Feces.		Total loss in excretions.		Intake in food.		Balance.	
	Nitrogen.	Uric acid.	Purin bases	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
March 22	6.6662	lost	0.0863	0.680	1.152	0.937	7.8182	1.6170	8.5754	4.4288	+ 0.7572	+ 2.8118
" 23	9.9552	1.9625	0.0618	0.7296	1.152	0.937	11.1072	1.6666	10.3262	4 1127	— 0.7810	+ 2.4461
Total	16.6214	.....	0.1481	1.4096	2.304	1.874	18.9254	3 2836	18.9016	8.5415	— 0.0238	+ 5.2579
Average	8.3107	1.9625	0.0740	0.7048	1.152	0.937	9.4627	1 6418	9.4508	4.2707	— 0.0119	+ 2.6289
					X-RAY PERIOD.							
March 24	7.6608	1.7437	0 0430	0.8640	1.229	0.993	8.8898	1.8620	8.5693	3.7003	— 0 3205	+ 1.8383
" 25	7.4480	1.6425	0.0654	1.1712	1.229	0.998	8.6770	2.1692	8.2309	3.8854	— 0.4461	+ 1.7162
" 26	7.9520	1.8490	0.0678	1.2800	1.229	0 998	9 1810	2.2780	9.1542	4.0788	— 0.0268	+ 1.8008
Total	23.0603	5.2352	0.1762	3 3152	3.687	2 994	26.7478	6.3092	25.9544	11 6645	— 0.7934	+ 5.3553
Average	7.6869	1.7430	0.0587	1.1050	1.229	0.998	8 9159	2.1030	8 6514	3 8881	— 0.3967	+ 1.7851

Average calories in daily diet: Preliminary period, 1230. X-ray period, 1230.

TABLE II. CASE I. IN PERIOD FOLLOWING DETERMINATION OF METABOLIC BALANCE, X-RAYS STILL BEING USED.

Date.	Nitrogen.	Uric acid.	P_2O_5.
March 27	6.1340	0.5422	1.2480
" 28	5 1744	0.5445	0.8442
" 29	3.3260	1 1236	0.4800
" 30	3.7796	1.4033	0.6144
" 31	4.9440	0.9035	0.6912

Died April 2d.

TABLE III. CASE 2. PRELIMINARY PERIOD.

Date.	Urine.			Feces.			Total loss in excretions.		Intake in food.		Balance.	
	Nitrogen.	Uric acid.	Purin bases	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.	Nitrogen.	P_2O_5.
March 24	8.8032	0.8925	0.0585	0.9744	1.684	1.737	10.4872	2.7114	12.2022	5.5623	+ 1.7130	+ 2.8509
" 25	8.1600	1.1390	0.0333	1.3008	1.681	1.737	9.8440	3.0378	12.5060	5.8678	+ 2.6620	+ 2.8300
" 26	9.2736	1.1320	0.0406	1.7220	1.684	1.737	10.9576	3.4590	12.8227	5.7196	+ 1.8651	+ 2.2600
Total	26.2368	3.1635	0.1324	3.9972	5.052	5.211	31.2888	9.2082	37.5309	17.1497	+ 6.2401	+ 7.9409
Average	8.7456	1.0545	0.0441	1.3324	1.684	1.737	10.4296	3.0694	12.5103	5.7165	+ 2.0800	+ 2.6469
					X-RAY PERIOD.							
March 28	14.3920	1.6750	lost	2.944	1.660	1.624	16.0520	4.568	11.5686	5.2803	— 4.4834	+ 0.7123
" 29	15.3300	1.5800	0.1103	3.246	1.660	1.624	16.9900	4.870	11.2949	5.4140	— 5.6951	+ 0.5440
" 30	14.6588	1.6180	0.1623	3.048	1.660	1.624	16.3188	4.672	11.4077	5.6659	— 4.9111	+ 0.9939
Total	44.3808	4.8730	0.3026	9.238	4.980	4.872	49.3608	14.110	34.2712	16.3602	— 15.0896	+ 2.2502
Average	14.7936	1.6243	0.1513	3.0793	1.660	1.624	16.4536	4.703	11.4237	5.4534	— 5.0298	+ 0.7500

Average calories in diet: Preliminary period, 1750. X-ray period, 1410.

TABLE IV. CASE 2. IN PERIOD FOLLOWING DETERMINATION OF METABOLIC BALANCE, X-RAYS STILL BEING USED.

Date.	Nitrogen.	Uric acid.	P_2O_5.
March 31	13.4064	2.0040	3.1392
April 1	14.0616	2.4274	3.0400
" 2	15.3216	1.9672	2.5920
" 3	13.9216	2.2811	2.9040
" 18	10.3320	0.8329	1.9488
" 19	12.4236	1.2219	2.9538

The condition of general nitrogen metabolism before *x*-ray treatment was begun is of interest in itself. The studies of von Noorden, Magnus-Levy, and A. E. Taylor have shown that in the ordinary course of chronic leukæmia nitrogen metabolism may show a balance, a slight loss, or a retention. It is not surprising that this is the case, for the clinical course of the disease would lead one to anticipate it. It is, however, an interesting contrast to the conditions in acute leukæmia, for most cases of the latter disease whose metabolism has been studied have shown a loss so large as to be but rarely equalled in other diseases. In a case recently studied by one of us the nitrogen loss through the urine was over twenty-two grams, and the whole loss was, indeed, much more than this if the nitrogen loss by hemorrhage be included.

The most interesting point in this connection, however, in regard to the cases now under discussion is the fact that both our patients during the preliminary studies of metabolism were very ill, and were rapidly growing worse, the first case in particular exhibiting fever, increasing prostration, and other appearances of a toxæmia that was hastening toward a fatal issue, and yet there was even in this case no evidence of excessive general tissue destruction, and in the second case there was a marked retention. The same point has been observed by others. Apparently, therefore, the toxæmia that occurs in the most severe stages of chronic leukæmia does not necessarily produce tissue loss. One would think at once of the possibility that in these cases a generous food allowance had sufficed to conceal the evidences of tissue loss, for it has been shown that abundant feeding in the course of toxæmias may at times transform the loss that usually occurs to a balance between the intake and outgo, or may even produce some retention. This, however, was certainly not the explanation in these cases, for, as can be seen from the figures, the amount of protein consumed was less than the normal, and the total value of the food, in calories, was very low. Hence it appears that in these cases there was severe toxæmia; and not only was there no evidence of any noteworthy increase in destructive processes, there was in one case actual decided retention that was probably due to the disease, an interesting contrast with most infectious toxæmias, with cancer, and with many nutritional diseases, such as exophthalmic goitre, Addison's disease, advanced diabetes, and gout (at the time of acute attacks). In the latter conditions, and in many other endogenous and exogenous intoxications, more or less marked nitrogen loss occurs, as an almost constant expression of the intoxication. It is uncommon, indeed, to find a marked toxæmia in which tissue loss does not occur; and hence the presence of a grave toxæmia associated with retention is the more interesting. Most of the amount that was

retained was probably used in making leukæmic tissue. It, of course, occurs to one at once that the retention was due merely to poor excretion, but this possibility does not seem of much consequence when one considers that our second patient promptly almost doubled her excretion when *x*-rays were used, and that the patient with acute leukæmia, whose case was mentioned above, excreted enormous quantities of solids, in spite of the fact that he had extremely severe kidney lesions. The patients at present under discussion had no evidence of nephritis, and there is no reason why they should have had marked incompetence of the excretory organs.

Another point seems to be clearly shown by the figures. The products of disintegration of leukæmic tissue do not appear to have any essential relation to the toxic symptoms that may occur in chronic leukæmia. Both our cases, while retaining nitrogen, were growing worse; one, immediately upon the beginning of very rapid tissue destruction, began to grow better; the other, having no increase of tissue destruction, continued to grow worse. Other cases that have improved largely upon the use of *x*-rays have almost certainly had tissue destruction similar to that which occurred in our successful case. The tissue that is destroyed in these cases is chiefly, if not entirely, the leukæmic tissue. Therefore we must, in this disease at least, restrict the idea that is so frequently expressed in connection with many nutritional disorders, that the toxic symptoms are chiefly due to the products of disintegration of tissue.

There are at times, however, symptoms of marked toxæmia in chronic leukæmia, especially in the later stages, and such symptoms were present in these cases, particularly in the first. It seems probable that these symptoms are produced either by products elaborated by leukæmic tissue in the ordinary course of metabolism, these products differing from those furnished by normal tissues of the same organs in being more toxic; or the symptoms may be due to poisonous substances elaborated in the course of the synthetic processes that go on during the actual building up of the leukæmic tissue. The former seems in many ways the readiest explanation of the symptoms, but the latter thought cannot be wholly dismissed, particularly when we consider that active increase in the splenic enlargement and in the number of leukocytes, is often coincident with signs of increasing toxæmia; while, on the other hand, if the disease is not progressing rapidly, there may be little or no evidence of intoxication, in spite of the presence, perhaps, of very extensive leukæmic deposits, and in spite, therefore, of the fact that these leukæmic deposits are playing a large role in the individual's metabolism. The first-mentioned conditions occurred in our cases before *x*-ray treatment, and both patients were then constructing tissue. When, in our second case, tissue destruction became largely in excess of construction, the toxic symptoms disappeared; but in the other case there was no increase of tissue destruction, construction apparently continued, and probably increased, and the toxic symptoms grew worse.

The condition of phosphorus metabolism is of interest because there was so marked a retention. A similar condition has been previously observed by Moraczewski, while some other authors have found a balance or a phosphorus loss. Taylor considers a phosphorus retention very surprising in the light of our knowledge of leukæmia. It does not appear to us to be so remarkable. Leukæmics whose disease is progressing constantly construct tissues that are rich in phosphorus, and naturally, if their tissue construction is largely exceeding the loss—and the condition of nitrogen metabolism shows that this was clearly the case in the second of our patients—there will be a retention of phosphorus in the construction of phosphorus-containing tissue; and, since leukæmic tissues are of the class that contain a large amount of phosphorus, the phosphorus retention is likely to be relatively large.

There are, to be sure, large deposits of leukæmic tissue in persons with leukæmia, and, since this tissue contains large amounts of nucleins, the excretion of products of disintegration of nucleins (uric acid, purin bases, phosphates) is likely to be high; and, as a matter of fact, these substances are, as is well known, usually found in large amounts in the urine of leukæmics. This large excretion does not mean, however, that retention of the constituents of nuclein-containing tissue cannot occur in these cases. It is apparently merely a question as to whether the construction or the destruction of these tissues is more active at the time of observation.

To turn to the effects of the *x*-ray, reference to the figures in the second case—the one that rapidly improved—shows a transformation upon the use of this treatment that was most remarkable in its extent, and particularly in the rapidity with which it occurred. The changes in the average daily excretion in the urine were as follows: The nitrogen rose from 8.7456 gm. to 14.7933 gm.; the uric acid from 1.0545 gm. to 1.6243 gm.; the purin bases from 0.0441 gm. to 0.1513 gm.; the phosphates from 1.3323 gm. to 3.0793 gm. The average increase was therefore as follows: nitrogen, 6.0477 gm.; uric acid, 0.5698 gm.; purin bases, 0.1072 gm.; phosphates, 1.7469 gm. The increase put in the form of percentage of the amount previously excreted was, in round numbers: nitrogen, about 70 per cent., uric acid about 60 per cent., purin bases about 260 per cent., phosphates about 200 per cent. The diet remained practically the same during this time. The monotonous food had, to be sure, become somewhat repulsive to the patient, and she refused to take quite as much as before; but consideration of this fact makes the result more striking, not less so, for normally reduction of the intake within reasonable limits is, of course, almost at once followed by

decrease of the outgo, while in this instance there was greatly increased excretion, in spite of somewhat reduced intake. The change in the diet was, however, of little consequence, and the amount of food remained sufficient to have maintained a distinct nitrogen retention had the excretion remained the same, but, as a matter of fact, the excretion became suddenly so largely increased that a previous decided nitrogen retention immediately became a very marked nitrogen loss. The break down of nitrogenous tissue produced by the *x*-ray was at least equivalent to the difference in the excretion in the urine before and during *x*-ray treatment, for, beyond the use of *x*-rays in the second period, there was no factor that was changed to any appreciable degree. As was stated, this difference in the nitrogen excretion was 6.0477 gm.; that is, about 70 per cent. of the previous excretion. Tissue break down was, however, almost certainly increased much more than 70 per cent., because much of the nitrogen excreted in the preliminary period was derived from the food, while all the increase in the *x*-ray period came from the tissues, since there was no increase of the food in this period. The last statement is true, also, of the uric acid, purin bases, and phosphates; the uric acid increase was about 60 per cent., that of the purin bases about 260 per cent., of the phosphates about 200 per cent.; but even these figures do not indicate the whole of the increased break down of tissues of the kind that yield these substances, for a large part of the excretion in the preliminary period was unquestionably derived from the food, particularly a large part of the phosphates. It may safely be said that the tissue break down in general was increased more than 100 per cent. in the three days immediately following the institution of *x*-ray treatment, and most of this increase occurred immediately. This statement, indeed, seems very conservative when one observes not only the figures for the urine, but more especially those for the balance.

After this time the intake of nitrogen and phosphorus could not be accurately determined; the subsequent figures are, therefore, less valuable, though they show clearly a marked further increase in uric acid excretion. Nevertheless, as far as it was possible to calculate them in the varied diet that the patient got after this period, the nitrogen and phosphorus in the food were found to be for some time, until the patient's appetite improved, decidedly below what they were when she was on rigid diet. Hence, there is little doubt that she actually had, for some days, at least, after we ceased determining the balance, an even more marked tissue destruction than she had during the time that the balance was known. However, the change that can be seen in the three days during which the balance was determined is sufficiently amazing.

It is a somewhat surprising fact that, although the phosphorus excretion showed an even more remarkable increase than did the excretion of nitrogen and uric acid, the phosphorus balance still showed that there was a retention even after *x*-ray treatment was begun. It is not possible to explain this definitely. The suggestions that most readily occur to one are that the patient, though breaking down nucleoprotein, was building up other tissues that contain substances, such as lecithin, that are rich in phosphorus; or that the products of the phosphorus-containing portion of the destroyed nucleoprotein were excreted slowly as compared with the nitrogen. The latter seems more probable. Nucleoprotein, in the course of ordinary digestion experiments, quickly breaks up (Umber) into albumin and nucleic acid. Albumin very rapidly undergoes further disintegration, while this apparently occurs more deliberately with nucleic acid; therefore most of the nitrogen from nucleoprotein would appear quickly, and purin bodies and phosphates more slowly. Evidence that this was probably the course of events in this case is seen in the fact that the uric acid excretion reached its height only after several days, while the nitrogen excretion rose at once to about the level that it maintained subsequently. Furthermore, after the patient was allowed her choice of food the intake was, as was stated, reduced much below the previous point, and at this period a rough calculation of the intake indicated a phosphorus loss. The phosphorus excretion represents the effects of the *x*-ray much more definitely than does the phosphorus balance in this short period.

As we have already stated, results as striking as those we have mentioned are, so far as we know, not produced by any other therapeutic agent unless the dose used is such as to give rise to acute toxic effects. In this leukæmic not only was the effect of *x*-rays not damaging; it was profoundly benign. There was a rapid tissue loss such as is seen in severe intoxications caused by infections and by many direct chemical poisons, and occasionally in nutritional diseases; but, instead of increasing the evidences of intoxication that were already present in this case, the process that produced the tissue destruction caused the appearances of intoxication to vanish rapidly, and the patient began quickly to regain symptomatic health. This condition of affairs is extremely striking in its contrast with common experience in other circumstances.

The results in the first case offer a remarkable comparison. They will be discussed somewhat further in considering the manner in which the *x*-ray acts, for they are of importance chiefly in that connection. At present it is of interest merely to refer to the fact that the figures show that *x*-ray treatment had no marked influence upon this man's metabolism. There was, apparently, a slight effort at increased metabolism, for the excretion of phosphates showed a noteworthy rise, and there was a slight loss of nitrogen, as shown by the nitrogen balance; but the phosphate excretion soon fell back

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in the period following the formal metabolism experiment, and, except for the fact that the uric acid excretion remained somewhat excessive, as it usually is in leukæmia, the excretion was persistently low; most strikingly low, indeed, for a man who was suffering from an intoxication so severe that it soon caused his death. This low excretion was, of course, largely due to a small intake of food, but this does not influence the fact that there was, at most, no noteworthy tissue loss.

As we have before remarked, our results in the successful case demonstrate in a very impressive way the profound power of the *x*-ray in influencing tissue processes. They show clearly that a very important effect, possibly the only important one, is an almost immediate increase in tissue destructive processes. This occurs not only in leukæmics, but in normal persons as well. Baermann and Linser have found an immediate, though less striking, increase in nitrogen metabolism in normal persons. They did not study the excretion of other substances, but Heile made some fragmentary and brief observations on the excretion of purin bases and uric acid in persons with various pathological conditions, and his results are in consonance with our own observations. Other studies made by one of us (Edsall, partly with Dr. Fife) in gout and in other conditions also show that the increase of metabolism is not confined to leukæmics, but they likewise indicate that it does not occur in all diseases.

There are certain conclusions that are of direct practical interest to be derived from the facts that have been discussed.

That acceleration of metabolism may be very useful in many obscure disorders of nutrition, in which there is apparently slow or imperfect disintegration of food or tissues, is a possibility that will be granted at once, and the effect of *x*-rays may properly be tried, with caution, in a considerable number of nutritional disorders, both because favorable clinical effects may perhaps be seen, and because a means of stimulating metabolism is something that has been much desired for purposes of investigation, and it may make it possible for the student of nutritional diseases to secure extremely useful knowledge concerning the nature and treatment of many of these diseases. There are already apparent, however, in previous clinical experience with *x*-rays, and in our own studies of metabolism, a number of facts which make it evident that the influence of the *x*-ray upon metabolism is likely to be limited in its clinical usefulness, and there are also facts which show that grave damage may result from the use of this treatment in some conditions, unless much caution is exercised. Some of these points relating to other disorders than leukæmia are not germane to the present discussion, and will therefore be referred to elsewhere; other points, however, and particularly those that relate to the dangers in the use of this agent, require some mention, since the emphasis that our study lays upon them and the new facts that it brings out are of direct importance to the clinician. Our results appear to demonstrate, too, the manner in which some of these dangerous results are produced, and indicate the necessity for especial caution in the use of *x*-rays when certain diseases are present.

It is not necessary to insist that any method of treatment that may cause a patient to double his tissue break down requires care in its use, if dangerous results are to be avoided. It is true that the tissue destruction produced in leukæmics is probably rarely, if ever, equalled in normal persons, and only infrequently in persons with other diseases. It is likewise true that vast numbers of persons have been exposed to *x*-rays with such usual absence of apparent general effects that there has until recently been little fear of any bad results, excepting purely local ones. But it should, at the same time, be kept clearly in mind that an effect so profound and unfortunate as is sterility may apparently occur readily, and yet the evidence that it has occurred appears only when deliberate investigations are undertaken to demonstrate that it has resulted. This makes one at once consider the possibility that other similarly unfortunate effects that are at present obscure may result. Certainly one can scarcely doubt that the sudden necessity for completing the disintegration of as large an amount of tissue as our second patient destroyed daily and the excretion of the end products of these tissues may prove to be a severe tax upon many of the organs concerned in metabolism, and upon the excretory organs, the kidneys in especial. It is not surprising to learn that severe kidney lesions have been produced in leukæmia, and even in other disorders. If Heineke's observations are correct, these kidney lesions are not the result of direct action of *x*-rays; and, if this is the case, our observations seem to demonstrate the reason for their occurrence. The increased excretion that our second patient accomplished shows what is demanded of a leukæmic who is successfully responding to *x*-ray treatment; and while this demand may safely be made temporarily of one whose organs are sound, there may be dangerous consequences with any patient, whatever his disease, if the labors of his excretory organs are suddenly doubled, when they are, perhaps, already taxed nearly to their utmost capacity.

The remarkable tissue destruction that we observed furnishes also a probable explanation of the curious toxic symptoms that have occasionally been noted after the use of *x*-rays. A sudden flooding of the organism with products of tissue break down may readily be sufficient in itself to cause intoxication, and it may also readily overtax the katabolic and excretory functions of various organs, and render them unequal to even their previous tasks. The

organism has such elasticity of function that harm probably results but rarely in persons whose powers are not already crippled, and evident harm has certainly not often been observed in any one. But the potentiality for harm certainly exists, and, while there is comparatively little knowledge as yet of such harmful effects, it must be remembered that the study of the dangerous general effects of *x*-rays has been arousing interest for but a short time, and, nevertheless, it has already proved surprisingly fruitful. Comparatively few conditions, too, have been studied in this connection, and broader investigation may develop further harmful effects, beyond those now known.

We would not be thought to desire to condemn offhand the use of *x*-rays. We believe, on the contrary, that the demonstration that *x*-rays may profoundly influence metabolism indicates the possibility of their good effects quite as forcibly as it shows the possibilities of bad results from them; and clinical experience has already clearly shown their great value in some conditions. We would, however, insist that the extent and importance of their effects upon tissue processes are just beginning to be appreciated, and that the power to produce such effects carries with it the power to produce great harm at times, unless the general manner of action is appreciated and the danger is carefully avoided. We are convinced that there has been too great freedom in the use of *x*-rays. Not that the sphere of their usefulness is likely to be narrowed; it will, on the contrary, probably be widened, but it should be widened by tentative trial of the effects in individual cases, and with careful watching for the evil results that are known to occur, and for others that are not yet recognized. So far as has been shown by studies of metabolism, by changes in morphology, or by clinical observation, bad general results are not likely to occur if the exposure is brief and the dose not severe; and the point of chief importance in avoiding danger seems at present to be the use of a very small dose and a brief exposure until, in individual cases, it is determined that harm does not result, the dose being subsequently increased slowly if desired. It is of equal importance, however, to watch alertly at the same time for evidences in the urine or elsewhere of resulting damage. It has not been a sufficiently general custom to follow such a plan, the chief point customarily observed having been the avoidance of burns. The determination of the dose and the exposure should not be left wholly to the *x*-ray expert, but should be largely reached through the attending physician's general knowledge of the individual patient; the evil custom that is so prevalent of merely sending a patient to an *x*-ray expert with a statement of the condition to be treated should cease, and both physician and *x*-ray expert should regularly consider the possible general effects, as well as the local, in the individual who is to be cared for. It seems not improbable that studies of the effect of *x*-rays upon excretion in various diseases, and, particularly, studies in individual cases that arouse apprehension, will prove a help in determining which diseases and which individuals may be treated with considerable impunity, which require very careful and deliberate progress, and which should not be treated at all by this agent. Certainly, however, there can be no doubt at present that the existence of nephritis should make one very cautious in using *x*-rays, and a good deal of care should also be exercised when there is already any form of toxæmia.

There is one point that has been dwelt upon chiefly by morphologists, and has caused a good deal of apprehension, that seems to us to be less an indication of danger than it is now generally thought to be. This is the widespread occurrence of necrosis in the lymphatic tissues in leukæmics and others who have been treated with *x*-rays. This is often considered evidence of the dangerous effects of *x*-rays, but its occurrence in leukæmia and in other diseases involving the lymphatic tissues appears to be actually evidence that the *x*-rays are accomplishing the purpose for which they are being used. Such changes show the necessity for caution, but instead of growing frightened about them one should probably consider them evidence of improvement in some diseases. The same effect is observed in the lymphatic tissues of normal persons, however, and in such persons, as well as in many diseases, it cannot be useful. How far extensive destruction of lymphatic tissue is a source of immediate danger to the normal organism is, as yet, unknown, but it is a striking fact that Heineke, in his animal experiments, saw no noteworthy symptoms that were evidently due to the destruction of lymphatic tissue, while later, when extensive bone-marrow changes occurred as a result of prolonged exposures, he did see very severe symptoms that resulted in death.

In concluding, we may refer to the manner in which *x*-rays act. It is not possible from clinical observation, or from studies of the morphological changes alone, to determine whether the effects are due to some physical or other direct influence of the *x*-ray, or to some peculiar response of the individual to stimulation of functions that lie within himself. It is, of course, known that some cases improve while other cases of the same diseases do not improve; and also that the individual leukæmic, for example, may at one time grow vastly better, and later show no effect; but such observations do not demonstrate the existence of reaction or lack of reaction of the individual, for they may be explained on the supposition that in any of these instances the *x*-ray is exerting a direct influence that is peculiar to itself, but the disease, in unfavorable cases, is progressing so persistently and rapidly that it keeps ahead, so to speak, of the effect of the *x*-ray.

Our studies, however, have shown clearly, we think, that

the influence is not direct, but is due to the power of the individual to respond to stimulation. This is of much interest from a practical standpoint, as well as a theoretical.

To make this point clear we would again refer to the fact that the one leukæmic who improved showed a striking effect upon metabolism during this improvement; while in the other case lack of improvement was associated not merely with evidence that the effect of the *x*-ray did not keep pace with the disease, but actually with evidence that there was practically no influence upon metabolism. Furthermore, Baermann and Linser, as was noted, have shown that the nitrogen metabolism of normal persons is decidedly increased by *x*-rays, and we have demonstrated the same fact, as well as a large increase of uric acid excretion, in a person whose metabolism was practically normal. In addition to this, we would mention with some emphasis the cases of gout previously referred to, in which nitrogen and phosphorus metabolism and uric acid and purin-base excretion were determined. It is an extremely striking fact that neither of these cases showed any distinct effect of *x*-rays upon metabolism. It is well known that patients with gout tend, as a rule, to have a very low excretion in the interval, while the excretion shows an apparently toxic increase with the attack. In each of our cases of gout, when metabolism was being studied in relation to the *x*-ray, the excretion was decreasing after an acute attack. It showed absolutely no increase, but actually continued to decrease when *x*-ray treatment was started, and this was repeatedly observed afterward. The changes that are usually seen in metabolism in gout continued to be present in these cases, therefore, and the course was apparently undisturbed by exposure to *x*-rays.

The facts that have just been mentioned demonstrate, we think, that the effect is not a direct one, but one that requires response on the part of the individual. It might certainly be anticipated that, if any destructive action is exerted directly by the *x*-ray, this action is more likely to occur with the tissues of a dying patient than with the tissues of one who is improving, but the patient that improved showed tissue destruction strikingly, while the patient that died showed none. This apparently cannot be explained in any way excepting upon the assumption that the patient that died was incapable of doing something that the other patient could do. The same explanation must be given for the fact that normal persons and leukæmics who are improving show increase of nuclein metabolism and general nitrogen metabolism, while our two patients with gout showed no effect. Only peculiarities in individuals can explain such results. This dependence of the favorable effect of *x*-rays upon individual reaction helps largely to explain the difference in the results in different cases. These differences are apparently not due so much to mere stubborn progress of the disease as they are to lack of that power in the individual which makes him capable of controlling the disease by responding to the stimulating action of the *x*-ray.

To be more specific concerning the processes that are stimulated and accelerated by the *x*-ray, we consider that it is highly probable that the action is chiefly upon autolysis. A considerable number of physiological and pathological body processes have, with great probability, been shown to be due to autolysis; that is, to activities that have the characters of ferment-like processes, and that produce in their course the same classes of substances as those found in the various stages of digestion. The view is now widely accepted that the exudate in pneumonia undergoes resolution as a result of sudden autodigestion, carried out not through bacterial influence, but through the activities of the tissues; the result in this case being due to a reaction that overcomes the effect of disease. In acute yellow atrophy and in phosphorus poisoning the liver, in particular, undergoes autodigestion, this being here apparently an important part of the progress of the disease. In involution of the puerperal uterus the excess of tissue is removed, in this instance for purely physiological purposes, by the same sort of autodigestion. These are conspicuous examples of fairly firmly established facts, illustrating the physiological and pathological importance of autolytic functions. Analogy with these and with many other similar facts that have been determined has led to the belief that katabolism in general is a ferment-like or digestive process.

Following, then, the general trend of thought, and the direction in which the results of recent experimental work pretty generally point, the most natural explanation of an increase in tissue destruction, when this increase is dependent upon individual body reaction, is that it is due to acceleration of autodigestive or autolytic processes. The remarkable suddenness and intensity with which the action of the *x*-ray begins, immediately after exposure, is more direct evidence in favor of the view that autolysis is influenced. This rapidity and intensity of action constitutes the most striking feature of the effect of *x*-rays upon metabolism. In our second leukæmic case, and in our normal subject, nitrogen and uric acid excretions were immediately greatly increased as a result of only five to eight minutes' exposure to *x*-rays. Baermann and Linser also saw an immediate influence upon nitrogen metabolism, and Heile observed the same effect upon purin bases and uric acid. Heile seems not to have controlled the diet and other factors, but this probably does not affect his results to any important degree. This extreme rapidity of action is a common feature with agents that influence ferments. It is also a most conspicuous feature in the resolution of pneumonia, in which disease the potential capacity to digest the exudate is apparently usually present, but is latent until some unknown factor causes it ordinarily

to become suddenly active, and then, within a brief time, a large mass of exudate is dissolved and disappears. In the suddenness and intensity of the change that occurs the effect of *x*-rays is closely analogous to the resolution of pneumonia; immediately after a brief exposure metabolism may proceed at double its previous pace, or, perhaps, even more rapidly.

Finally the analogy between the effect of radium and that of *x*-rays is so close that the probability that *x*-rays accelerate autolysis becomes nearly a certainty when one considers that Neuberg has demonstrated, *in vitro*, that radium has this influence.

References.

Albers-Schonberg. Münchener medizinische Wochenschrift, 1903, No. 43.

Heineke. Mittheilungen aus dem Grenzgebiete der Medizin und Chirurgie, Bd. xl., Heft 1 and 2.

Von Noorden. Lehrbuch der Pathologie des Stoffwechsels.

Magnus-Levy. Virchow's Archiv, Bd. clii.

Taylor. Contributions from the Wm. Pepper Laboratory of Clinical Medicine, 1900.

Moraczewski. Virchow's Archiv, Bd. cli.

Baermann and Linser. Münchener medizinische Wochenschrift, 1904, No. 23.

Heile. Zeitschrift für klinische Medizin, 1904.

Neuberg. Zeitschrift für Krebsforschung, 1904.

FRACTURES OF THE HEAD OF THE RADIUS. AN EXPERIMENTAL STUDY AND REPORT OF CASES.*

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The writer's interest in this subject was excited by an obscure injury of the elbow-joint, which came under his care about two years ago. The skiagraph revealed a complete fracture of the external lip of the head of the radius, with almost perfect apposition of the fragments. The difficulty in diagnosis and the uncertainty in prognosis, since the fracture was an intracapsular one, led me to make a search of the literature, which proved to be very interesting, though scanty. In February of this year I was asked by a physician to take charge of an injured elbow in one of his patients, which also proved to be a fracture of the head of the radius, the anterior portion of the head being separated. My search of the literature showed that only eight cases had been diagnosed during life by the clinical signs. In every one crepitus had been detected over the radial head. I have the first case to be recorded in which the diagnosis was made without crepitus, mobility of the fragments, or deformity.

The chief objects of this paper are to show that the fracture is typical and frequent; that the most common form does not give the pathognomonic signs of fracture, to show why it does not, to outline the symptoms by which it may be recognized, and to show that, in spite of good authority to the contrary, operation will rarely be required.

The plan of the paper includes a report of my own cases, with reference to three others, a *résumé* of the literature, a report of the experimental work, and a general study of the fracture under its anatomy, frequency, mechanism, diagnosis, prognosis, and treatment.

Case I.—July 18, 1903, Mrs. R., aged thirty-nine years, while stepping from a porch tripped over a bicycle, striking on her left side. She could not say, definitely, what part of her body first struck the ground, but thought that it was her left elbow. A doctor was called in immediately, but could not make a diagnosis, and advised her to have a skiagraph taken. I saw her on the following day, before the *x*-ray had been employed, and made the following observations: The elbow was vaguely but not greatly swollen. The condyles of the humerus, the ulna, and the radius seemed to be normal in position, and no deformity could be detected. There was very marked pain and tenderness below the external condyle of the humerus and about the head of the radius. Flexion and extension were much limited by pain; pronation and supination produced still greater pain, but were possible, and the head of the radius was shown to be normal in position and to move with the shaft. No crepitus was detected at any time. I suspected a serious injury of the joint, but could not tell what it was. The skiagraph showed a fracture of the external portion of the radial head, in good apposition, in spite of the fact that the elbow had not been immobilized since the accident, twenty-four hours before, and the manipulations necessary in both examinations. Something evidently was acting as a most efficient splint. My attention was at once directed to the orbicular ligament as the splinting structure.

The limb was dressed, for the first twenty-four hours after the diagnosis was made, in the acutely flexed position, with the forearm across the chest. The patient complained of so much pain from this position that an anterior right-angled splint was applied. Gentle massage was begun a few days afterward, and at the end of two weeks gentle passive motion. When the splint was removed, at the end of the fourth week, interference with motion was marked, but there was some

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slight movement in all directions. In the hands of a masseur this was made to disappear largely in a few weeks. At the present time the return of function is almost perfect. A very slight loss of extension is present, so slight that the patient did not appreciate it until her attention was called to it.

Case II.—Miss S. F., aged thirty-eight years, trained nurse, on the evening of February 28, 1905, fell down a flight of steps. She does not know which part of the body struck first, but has a distinct recollection of thinking of her neck at the time, and of putting forward her arms to save it. She thought her right elbow was flexed over her head, in which case she would have struck on her elbow. The thenar and hypothenar eminences of both palms were bruised, particularly those of the right hand.

I examined the elbow about twenty-four hours after the injury. The right elbow was swollen, but not excessively, and was somewhat œdematous, the swelling and œdema being most marked on the outer side. The pain was marked, especially on movements of the elbow. A systematic search was made to locate the exact seat of the injury. Measurements from the acromion to the external condyle showed no shortening. The lower end of the humerus of the affected side was carefully palpated, including the condyles, without giving any signs of fracture or much pain. A careful examination of the ulna throughout, and of the radius up to the neck, was made without disclosing any signs of fracture. When, however, the head of the radius was touched the patient complained of very great pain, and said at once, "That is the place." With a finger on the head of the radius, the forearm was pronated and supinated to determine the continuity of the head with the shaft. The head clearly moved with the shaft, but the pain was excruciating, and the limitation of motion very marked. When the patient attempted to produce pronation and supination voluntarily, she failed to produce any movement, on account of the pain induced by the effort.

A diagnosis of fracture of the head of the radius was made, and was verified by the skiagraph, the anterior part of the head being broken off, and slightly pushed toward the hand. The position of the forearm was in flexion and midway between pronation and supination. An anteroposterior view showed no sign of fracture; the lateral view showed it very clearly. The coronoid process was intact.

The limb was immobilized in right-angled flexion by an internal splint. At each dressing the joint was moved within the painful limit, but never forced. In about ten days the patient was able to produce about as much motion voluntarily as I could by handling the parts.

March 10*th*, about four weeks after the accident, the splint was removed, and the following observations made: From the right-angled position about 15 degrees of flexion and the same extent of extension were possible. When any force was added to increase the extension, much pain was induced. The forearm was in pronation, and supination could not be carried beyond the mid-position. Nothing abnormal could be detected in the head as it rotated.

April 9*th*. The patient has been in the hands of a masseur since March 23d, about eighteen days, and has received a treatment of about a half-hour's duration every day. Pronation and supination have returned almost completely. Extension lacks about 50 degrees of being complete, while the flexion has progressed about as far, although the limitation in this direction is much less noticeable. The masseur, during each treatment, forces the elbow into nearly complete extension, and in flexion makes her touch her own shoulder on that side.

12*th*. The patient came here direct from the masseur to-day. The improvement in the last few days is marked, especially in the direction of extension, but I believe this is largely due to the fact that the joint has not had time to stiffen after the masseur's forcible movements, as in previous visits. With her arm resting on a table, and an ordinary flat-iron in her hand, she is able to bring her forearm almost in contact with the table. There is considerable ecchymosis on the inner side of the joint, and there is felt, for the first time to-day, a slight but decided crepitation by the finger over the head of the radius, on rotation.

14*th*. Three skiagraphs have been taken since the last visit, in various positions of the elbow, but none of them show a line of fracture. The exposure in one of them was almost the same as that which showed the fracture just after the accident. Not one of these skiagraphs, however, is clear; so that the absence of a fracture line is not proven.

July 31*st*. The injured arm now shows almost full function. Extension is not quite as full as in the normal elbow, but a little force overcomes the deficiency. Rotation is apparently as good as ever. The patient has been out nursing a case since I last saw her, and she suffered no inconvenience from her arm while at her work. The crepitation or click over the head of the radius has almost entirely disappeared. Two skiagraphs were taken two days ago, by Dr. Pancoast. One was a lateral view, with the forearm in pronation; the other, an anteroposterior view, with the forearm in supination. They both show clearly the line of fracture on the upper surface of the head, and a slight depression of the small fragment. According to my interpretation of both plates, the detached fragment in supination is posteroexternal. It is impossible to decide from the skiagraph whether union has occurred or not, although it is a good one, showing the texture of the bone, and is taken almost in the line of fracture.

The favorable progress of the case toward full function, which is just as marked as in the first case; the absence of pain and tenderness, and of any disturbance in the joint,

would tend to show that union had occurred. On the other hand, the detection of the click or crepitation over the head on rotation, coincidently with the ecchymosis, swelling and severe pain about the elbow, would tend to show that the forcible movements of the masseur had produced a refracture. I am inclined to believe that fibrous union occurred during the period of rest following the accident, that the masseur caused a refracture, and that now the fragments are again adhering to each other, or that the approximated fractured surfaces are becoming more or less smooth from friction. The patient is well satisfied with the result, and I see no reason for even considering the advisability of an operation.

In a study of fractures of the head of the radius, one is impressed at the outset with its remarkable obscurity, and, as a result of this, its very scanty literature. Gant's surgery[1] says: "Fracture of the head of the radius occurring alone has, I believe, never been met with. In conjunction with fracture of the coronoid process, it has occurred in two instances, both in the same subject."

Berard,[2] in 1834, reported the first case, which he discovered postmortem; and, as late as 1893, Ashhurst[3] states that "fracture of the head of the radius is a rare form of injury which does not appear to have been recognized during life, though the possibility of its occurrence has been demonstrated by dissection."

Bruns,[4] in 1880, collected twenty-one cases from the literature, in twenty of which the fracture had been proven by anatomical investigation. He said nothing of the case not so confirmed. He reported a case also demonstrated by postmortem dissection.

Our text-books on surgery give it only passing notice, from which we may assume that it is still considered to be very rare.

Since the advent of skiagraphy into the field of surgery, we have learned of many fractures of comparatively frequent occurrence that were previously overlooked. They are usually fractures of small bones or bony prominences, particularly about joints, and in some instances have been shown to be sprain or tear fractures. These are due to the separation of muscular or ligamentous attachments, resulting from sprains or fractures with which sprains are associated. For instance, in Pott's fracture of the fibula the internal lateral ligament of the ankle remains intact and tears off the tip of the internal malleolus, and the inferior tibiofibular ligament partially separates the adjacent surface of the tibia. Fractures of the head of the radius cannot be placed in this class, since no ligament is attached to it except a very thin reflexion of the capsule.

The skiagraph, however, has not done away with the necessity for an accurate diagnosis based on the clinical signs. The great majority of physicians are still without the opportunities for the general use of the skiagraph. The cost of the necessary apparatus, and the skill required in the interpretation of its shadows, will compel the average doctor, for many years, if not always, to depend on his sense of touch and his previous experience in similar cases. Moreover, in the hands of the best skiagraphers there are many cases in which the skiagraphic evidence is, at least, doubtful, and the clinical signs more positive.

In a longitudinal fracture of the head of the radius, the approximation of the fragments is often so close that a skiagraph might fail to show it, especially if the plate is an obscure one, or the exposure made in the wrong direction.

It has been said that by taking two pictures at right angles to each other, it is practically impossible for even the slightest fracture to escape detection, taking for granted, of course, that the technique is not at fault.[5] But the technique is often at fault, as anyone may judge who sees many skiagraphs of fractures.

In my second case the anteroposterior exposure showed no sign of fracture. The lateral exposure gives a picture showing almost through the line of fracture. There is an appreciable separation and slight depression of the detached fragment. This depression appears to be frequent, and was present to a slight degree in my first case also. A fall on the hand would readily account for it. In one or two of the experimental fractures the approximation was closer, and the depression absent. How much influence hemorrhage from the fractured surfaces would have in separating the fragments is, of course, problematical. The closer the approximation and the less the depression, the more difficult will be the detection of the fracture by the *x*-ray. If the line of fracture is wedge-shaped, as in several of the experimental fractures, the line of fracture on one side of the wedge will be directly over that on the other side of the fragment, the two lines of fracture then confusing each other. The direction of the rays would not, then, be in the line of fracture, which would be further obscured by being taken through bone. I am convinced that many of them do escape detection even by the skiagraph. In one case from the literature (Gordon, No. 42) the skiagraph showed only fracture of the neck, the fracture of the head being found only after its excision. It becomes very important, therefore, to diagnose as nearly as possible the exact seat of injury, and to so inform the skiagrapher, who will then be on the lookout for it.

CASES FROM THE LITERATURE.

1. Berard.[2] A man, in committing suicide, threw himself from a second-story window. The elbow presented all the signs of a dislocation backward. Reduction was easy, in spite of the cadaveric rigidity. A little pressure on the arm and forearm, in opposite directions, sufficed to reproduce

the displacement, which was attended by a slight crepitation. Dissection showed a fracture of the coronoid process, and another which, splitting the head of the radius, extended obliqely downward one-half inch, upon the anterior face of the bone, and separated about the anterior one-third of the articular surface.

2. Velpeau.[6] A man, aged fifty years, dislocated his elbow in a violent fall. This was taken for a contusion. At the end of six weeks, not recovering the use of his arm, he consulted M. Velpeau, who recognized the dislocation. Ineffectual attempts were made to reduce it. After a fatal attack of erysipelas, an autopsy revealed, besides a dislocation, a transverse fracture of the anterior two-thirds of the head of the radius.

3. Malgaigne.[7] The patient fell from the second story, on his elbow, and the injury seemed to be only a transverse fracture of the olecranon. The patient died on the fifty-eighth day after the accident, and the autopsy revealed a comminuted fracture of the apophysis of the coronoid process, and of the head of the radius.

4. Malgaigne.[8] Eight days after, Malgaigne reduced a dislocation of the head of the radius forward; the patient, an old man, left the hospital. He returned five weeks later, to die of pneumonia, forty-seven days after the reduction of the dislocation. The synovial membrane was of a dark-red color, and was covered with blood clots and false membrane. An incomplete fracture separated about the posterior fourth of the radial head. It showed no trace of reunion.

5. Verneuil.[9] An adult fell from a height and received several grave injuries, from which he died. Both radii were fractured at their lower ends. Almost by chance an incomplete fracture of the head of the radius on the right side was discovered. There was one vertical line of fracture about 1 cm. deep, dividing the head into two nearly equal fragments, one anterior and the other posterior. The second fissure, also vertical and perpendicular to the first, divided the anterior fragment into an internal and an external part. The fragments were in contact with each other.

6. Hodges.[10] Hodges found a case in the dissecting-room. It was therefore without a history. There was a fracture of the radius at the junction of the upper and middle thirds of the shaft. A small fragment of the head, three-eighths inches in diameter, was chipped off. The fragment has a well-defined outline, and is united in position without any signs of new growth of bone around it. The muscles of the forearm are atrophied and rotation of the forearm impaired, but this was due to the fact that the upper fragment of the broken shaft of the radius was twisted on the lower fragment, the bicipital tuberosity looking forward instead of inward.

7 and 8. W. H. Flower[11] refers to two specimens of fracture of the coronoid process in the museum of St. George's Hospital. In both specimens the head of the radius was split longitudinally. They were taken from the body of a man killed by a fall from the roof of St. George's Hospital. There was a posterior luxation of the bones of the forearm backward, and fracture of both coronoid processes. The specimens are now preserved in the museum of the hospital.

9 and 10. Hamilton[12] refers to two specimens in Dr. Mutter's cabinet, of fracture of the outer half of the head of the radius. In one case the small fragment was displaced downward in the direction of the axis of the bone, and in the other the fragment was thrown outward or to the radial side. Both were firmly united in their new positions.

11. S. D. Gross[13] calls it a rare form of fracture, and refers to a specimen obtained from the dissecting-room, in which a portion of the head of the radius was chipped off, and has become permanently united to the contiguous border of the coronoid process of the ulna.

12. Gurlt.[14] in his work on fractures, gives an illustration of a specimen in the museum of the University of Edinburgh (No. 60), of a healed fracture of the external condyle of the humerus and the head of the radius, with ankylosis of the elbow-joint. The head of the radius was split longitudinally about one and a quarter inches, and at its lower end transversely. The two fragments showed a fork-shaped divergence above, and were united to the external condyle by callus. The ulna was also united to the humerus and upper part of the radius by callus.

13 and 14. Weichselbaum.[15] By accident the writer found in each elbow-joint in the body of a twenty-year-old, strong, young soldier, who had died of dysentery, a free foreign body, and a corresponding loss of substance in that part of the radial head articulating with the ulna, showing that on both sides a fracture of the radial head had occurred.

15. Von Lesser.[16] A nineteen-year-old sailor fell from the mast, striking on the left elbow, which was strongly flexed, and on his nose, which was broken. Above the right olecranon was a small, penetrating wound. This was united by sutures, the physician thinking the injury to the joint only a contusion, because he could not reach the joint with a probe. A purulent discharge later escaped, and von Lesser excised the elbow. Upon examination of the radius it was found that the anterior and inner part of the head had been broken off, but still retained an attachment to the neck by a lamella of bone. There was a considerable cleft between the two fragments of the head.

16. Hodges.[10] A man, aged twenty-one years, received a charge of small shot in the left arm. The integument and muscles near the elbow-joint were torn for a space of about six by four inches, and the bones of the elbow broken, although not by the shot, only a few of these penetrating deeper than the soft tissues. The arm was amputated seven hours after the accident. Recovery followed. The specimen is now in the Warren Museum, and shows the head of the

radius split into three nearly equal parts, one of which is detached and lost. It is a multiple longitudinal fracture, with one of the divisions extending downward for an inch on the side of the neck and shaft of the bone. The tip of the external condyle is broken off. The ulna is uninjured.

17. Bryant,[17] in his *Practice of Surgery*, shows a drawing of a longitudinal fracture of the head of the radius, accompanied by a fracture of the coronoid process, the specimen being taken from a woman aged seventy years, whose arm was amputated for a compound fracture of the elbow, caused by a fall.

18. Hodges.[10] A man fell sixty feet, and died in six hours. The essential features of the injury to the elbow were diagnosticated, because of the slight swelling (essential features not mentioned). The postmortem examination, however, revealed a longitudinal fracture through the head of the radius, without displacement. This was not detected during life. An oblique fracture of the ulna, the olecranon being included in the upper fragment, was present. Had the line of fracture turned anteriorly instead of posteriorly, it would have been a fracture of the coronoid process.

19. Hodges.[10] A man aged twenty-four years, machinist, was thrown against machinery, fracturing the right elbow and opening the joint. He entered the Massachusetts General Hospital one hour after the accident. The external condyle was broken off, and with it a segment of the head of the radius, equivalent to one-third of its surface. The joint was excised and the patient recovered. The specimen is now in the Warren Museum. There was no comminution of any of the bones, the fracture being confined to the head of the radius and the external condyle. The ulna was uninjured.

20. Hodges.[10] A man, aged forty years, fell forty feet to a brick pavement, sustaining a compound fracture of the elbow-joint. The specimen, which is now in the Warren Museum, was obtained by an excision of the elbow-joint before the patient died on the following night. The head of the radius is split into two unequal parts, neither of which is detached, nor does the fracture extend into the shaft of the bone. The olecranon and coronoid process are broken from the shaft by a somewhat spiral fracture, and the last-named process into two portions longitudinally. The humerus was uninjured.

21. Adams.[18] A man died forty-eight hours after a fall from a great height. He suffered from a simple fracture of the right femur, a compound fracture of the left femur, a lacerated wound of the scalp, and a fracture of the right radius. Distinct crepitus was felt during life over the head of the radius, but the head moved during rotation. Upon dissection the capsular ligament was found to be torn slightly posteriorly, and a portion of bone lay in the opening. It was necessary to cut away the capsule to show the entire extent of the fracture, which was as follows: The outer one-third of the head was split away from the inner portion in a vertical direction, and was divided into two pieces. The lines of fracture appeared to be abruptly terminated by the orbicular ligament. The cartilage on the articular surface of the humerus was abraded, leading one to suppose that the head of the radius had been driven against it and thus split.

22. Hodges.[10] A man, aged fifty-five years, was engaged in loading stone. A heavy mass fell on his right arm, producing a compound comminuted fracture of the elbow-joint. Excision of the elbow was performed at the Massachusetts General Hospital twenty-four hours after the injury. The patient recovered, and the specimen is now in the Warren Museum. The head is divided into three nearly equal parts, by a fracture whose lines radiate from the centre of the articular surface, and, passing downward, have split and comminuted the neck and shaft of the bone for one and one-half inches in extent. One of the three divisions of the head have been lost. The external condyle of the humerus has been broken off. The ulna was uninjured.

23. Huter.[19] Two-thirds of the radial head in a young woman was broken off by a fall on a sharp corner. The detached piece of bone lay as a free movable joint body at the posterior side of the joint, close to the outer border of the olecranon. This disturbed considerably the movements of the joint, so that the patient was unable to work. After a free incision, using a Lister spray, the loose body was extracted. It was still attached to a strand of the capsule, which had to be divided. The wound was sutured and healing without inflammation followed, with a full return of function.

24. Trelat.[20] A man, aged twenty-two years, fell, holding his hands forward and striking on his palms. He suffered only in one elbow, in which the movements were possible, but very painful and limited. There was a certain amount of deformity at the elbow, and later ecchymosis and effusion into the joint were evident. Crepitation was felt over the radial head, and pain on supination and pronation. Fracture of the head of the radius was diagnosed on these symptoms.

25. Bruns.[4] A man, aged forty years, fell from a scaffold a considerable height, and died in a short time as a consequence of a fracture of the skull and a contusion of the brain. The right arm shows several injuries. Besides a wide tear in the capsular ligament, there was also a tear in the annular ligament. A third of the radial head was broken off, corresponding to the anterior portion of the same in the mid-position between pronation and supination. The line of fracture extended as far as the border between the upper cartilaginous surface and the neck, the detached fragment hanging by a strip of capsule at the inner half of the joint. The joint between the humerus and ulna was intact. There was, besides the fracture of the radial head, an oblique

fracture of the humerus at the junction of the lower and middle thirds, and a fracture of the middle of the ulna.

26. Pinner.[21] The patient fell on both palms, with arms extended. The accident was at once followed by weakness in the right hand and forearm, but no impairment of motion apparently. In one hour severe pain and swelling occurred in the elbow-joint. No displacement was discovered, owing to the fat and much pain present. Localized pain and tenderness at the upper third of the radius led to a diagnosis of fracture there, and the arm was dressed in full supination. On the next day, when the swelling had subsided, acute pain and tenderness were found over the head of the radius. The head rotated with the shaft, but limitation of pronation and supination were present. There was also paralysis of all the muscles supplied by the posterior interosseous nerve. The joint was fixed for four or five weeks, after which electricity was employed, and finally full movement of the hand returned.

27. Pinner.[21] This consisted of an anatomical specimen from the Pathological Institute of Freiberg, and was from an adult. One-half of the head was broken off, and remained attached to the capsule. The fractured surfaces, instead of uniting, have formed a false joint by eburnation.

28. Stimson.[22] A delicate, strumous lad, aged thirteen years, was struck on the outer side of the right elbow. Two months later he was admitted to the hospital with a suppurative arthritis of the same elbow. Stimson excised the joint and, in the course of the operation, found the outer half of the head of the radius separated from the rest and from the shaft, with an irregular surface of fracture and preservation of the articular cartilage. There was about a half-ounce of thick, brownish pus in the cavity of the joint, and the articular cartilage of the ulna was eroded and hanging in shreds. The skin was normal, except for some reddening over the head of the radius. There was complete muscular fixation of the joint at a right angle, and swelling of the posterior and lateral regions. Rotation of the forearm was painful and very limited.

29. Stimson.[22] A man, aged twenty-seven years, was admitted to the Presbyterian Hospital April, 1882, with a backward dislocation of the right elbow, produced by a fall from a wagon upon the palm of the hand. Stimson reduced the dislocation under ether, and then felt a movable piece of bone on the outer side, between the olecranon and the head of the radius. As the olecranon, external condyle, and accessible portion of the radius appeared uninjured, it was thought that the movable fragment must be from the inner side of the head of the radius. It was removed with antiseptic precautions. It represented about one-third of the head of the radius.

30. Stimson.[22] Dr. W. R. Townsend treated a case of supposed fracture of the head of the radius in the Bellevue Hospital, in 1881. The patient was a stout, muscular man, aged thirty-nine years, who fell from a ladder, striking on the outer side of his left forearm, which was held close to his body. After the swelling had subsided a movable piece of bone could be felt at the side of the head of the radius, and crepitus could be felt as the wrist was rotated. The diagnosis was confirmed by Drs. McBurney and Yale. Stimson saw him a year later, in April, 1882; flexion of the left elbow was complete; extension incomplete to about 140 degrees; pronation and supination limited to about 90 degrees; some pain in damp weather. The head of the radius is very irregular, its diameter greater than usual, and the distance from its upper edge to the top of the olecranon nearly an inch greater than on the right side. The prominent part of the radial head moves nearly an inch on rotation of the wrist. The edge of the outer condyle of the humerus feels a little irregular. The arm was strong and useful, and the patient has returned to duty in the fire department as a steersman of a hook-and-ladder company.

31. Roberts.[23] A woman, aged fifty years, fell and injured her left elbow. She was examined by the members of his class at the Polyclinic Hospital. At one time the head of the radius seemed to move with the shaft, and the next moment not. Finally Dr. Roberts elicited motion and distinct crepitus when he placed both thumbs side by side on the head of the radius, and made alternate pressure, with the one and the other. He made a diagnosis of fracture of the head of the radius, and thought that the previous uncertainty was due to the fact that the examiner's finger was placed sometimes on the detached fragment, and at other times on that part still connected with the shaft of the radius. A splint was applied merely to keep the parts at rest, as there was no tendency to displacement. The woman was told to report the next day, but never returned.

32. Moullin.[24] The specimen, which was shown before the Pathological Society of London, came from a boy, aged sixteen years, whose arm was crushed by a machine accident. The external condyle of the humerus is broken into two or three pieces, and there is a deep depression in the capitellum leading into a fissure. The upper epiphysis of the radius is completely detached, the line of separation passing between the cartilage of the extremity and the diaphysis; otherwise it is not injured, though the orbicular ligament is torn away. The synovial membrane of the joint still retains its connection with the head of the radius. Amputation was performed a short distance above the elbow-joint. The hand was uninjured, the whole of the violence falling on the outer side of the elbow and forearm.

33. Wainwright.[25] A man fell from a ladder twenty feet on his right hand. Upon examination there was much pain and effusion in the right elbow-joint. All movements of the joint were limited. There was no dislocation, and the shafts

of the radius and ulna were felt to be intact; but, owing to the swelling, it was difficult to be sure that the head of the radius moved with the shaft. On deep pressure distinct crepitus and much pain were obtained. Wainwright was not aware that the head of the radius could be fractured, and so diagnosed fracture of the neck. Thirteen weeks afterward the condition was as follows: The measurement between the condyles was one-half inch wider on the affected side. The external condyle was ill-defined. The head of the radius rotated with the shaft, but appeared not to be in line with it, rather making an angle with it. Flexion and extension could be performed only through an angle of 30 degrees, while pronation and supination were reduced about one-half. He was quite unable to work. An operation later showed the head to be split into two nearly equal parts by a vertical cleft filled by fibrous tissue. The coronoid process was also separated.

34. Stimson.[26] A man was brought to the hospital with an injury of his left elbow, the cause of which was unknown. There was considerable swelling and tenderness. The head of the radius projected externally, and there was crepitation on rotation. On supination it projected still farther laterally. With the elbow at a right angle the forearm could be moved backward and forward about a quarter of an inch, indicating probably a fracture of the coronoid process, with or without a rupture or avulsion of the orbicular ligament, in consequence of which the radial head was free to move. The elbow was flexed at a right angle, and put up in a plaster cast for three weeks, when no improvement was found. Arthrectomy was performed, and the following condition was present: The coronoid process was broken off at its base; the head of the radius was split anteroposteriorly, and the inner half was broken into two pieces, one of which was displaced forward and lodged in the anterior ligament. The neck was crushed in such a way that the upper surface formed an oblique angle with the shaft. The patient made a rapid recovery, and the plaster cast had just been removed. He had a range of movement of about a right angle. Pronation was complete, but supination was limited.

35. Bennett.[27] A specimen was obtained from the body of an elderly woman in the course on operative surgery in the School of Physic. No other fracture of the forearm or humerus was associated, nor was there any evidence of dislocation. The line of fracture in the cartilage was clearly marked. It divided the cup-shaped depression into two almost equal parts, and passed downward on either side through the surfaces, articulating with the lesser sigmoid cavity of the ulna and the coronary ligament. It could be indistinctly traced on the corresponding surfaces of the neck of the bone. There was no projection of callus on any part of the line of fracture, but union by bone was firm. The anterior half had evidently been detached and slightly depressed below its fellow.

36. Delorme.[29] The patient, a soldier, fell in a casemate from a height, the elbow striking the ground on the posteroexternal aspect. At the moment of impact the patient heard a cracking sound. The movements of the elbow rapidly became painful, especially on extension, and a swelling soon appeared on the internal aspect of the forearm and the posteroexternal surface of the elbow. Delorme examined the patient three days after the injury. Ecchymotic swelling covered the internal aspect of the forearm almost entirely, and was encroaching on the anterior surface. The posteroexternal part of the elbow presented only a slight degree of ecchymosis, without notable swelling. The signs at first seemed to indicate a sprain, but in manipulating the parts crepitation was detected, and this localized Delorme's attention to the head of the radius. In pressing on the external part of the head from before backward he produced the crepitation, and he concluded that it was produced by a fragment representing the external third of the circumference of the head, which could be displaced forward and backward by seizing it between the finger and thumb. During repose it conformed well with the radial head without deformity, but during the displacement the crepitation was more clear. All the assistants established its presence. It was better appreciated during pronation and supination. Nothing like it could be produced in the other arm. After a month of immobilization he concluded that consolidation had occurred, since he could not then produce crepitation. Later full motion and power returned.

37. Cheyne.[28] Miss S., aged twenty-six years, was thrown from a carriage on her left elbow, and, in overturning, again struck in about the same place. Fracture of the shaft of the radius was diagnosed, and treated for four weeks with anterior and posterior splints. At the end of that time the forearm was completely pronated, and supination was impossible. The forearm was almost completely extended, the range of movement was very slight, and attempts at movement were very painful. Cheyne saw the elbow about seven weeks after the accident, when the condition had not improved, and a loose fragment of bone could be felt at the posterior part of the joint, between the olecranon and the head of the radius. A few days later the loose fragment, which represented about half of the head, was removed by operation. The wound healed by first intention, and the return of function was almost perfect.

38. Cheyne.[28] With the above case, Cheyne reports a second resulting from the kick of a horse. The loose fragment was excised. Healing by first intention followed and much improvement of function by the time the patient left the hospital.

39. Stimson.[31] The patient in trying to save a child from falling had sustained an injury which had been diagnosti-

cated as a dislocation. After two weeks' treatment he came under Stimson's care. Upon examination there was found a prominence at the upper aspect of the elbow, and this seemed to be a portion of the head of the radius. An operation verified this opinion. At the time of the operation the patient had lost the power of flexion and extension of the forearm, and almost entirely that of rotation. Motion is now very fair.

40. Stirling.[30] A young sailor had his right arm crushed between the buffers of cars so badly that amputation was necessary. On examination of the bones afterward the only injury found was that to the head of the radius. The outer half of the hollow of the head was chipped off, and was found loose in a quantity of fluid below the joint. The ulnar side of the cup, as well as the facet for articulation with the ulna, was deeply fissured. The neck of the radius was uninjured.

41. Jayle.[32] A man, aged sixty-two years, was run over by a vehicle, causing him to fall on his elbow. Fracture of the olecranon was diagnosed. The patient died suddenly and at autopsy the examination showed a fracture of the olecranon, a fracture of the neck of the radius, and the radial cup divided into three fragments, two of which were very small.

42. Gordon.[33] A man, aged forty-five years, fell from a high cart and struck on the ground, with his outstretched hand. Before he could rise the horse struck him on the right shoulder, throwing him violently on the right elbow. A posterior dislocation and a Colles fracture resulted. Much crepitus was detected at the elbow, but the swelling prevented a complete diagnosis. A month later the ankylosis and bad position, with the pain, made the limb almost useless. At this time there were no distinctive signs of fracture, except crepitus over the upper end of the radius. A skiagraph showed only a fracture of the neck of the radius. To improve the motion of the elbow-joint, an operation was done, which consisted mainly of removing the head of the radius. This was split vertically into two nearly equal parts, both of which were separated from the shaft of the radius. The result of the operation was satisfactory. Almost all the movements of the joint returned except for supination, which could not be carried beyond the mid-position. The fragments were quite united at the time, and one was ankylosed into the lesser sigmoid cavity of the ulna. Gordon thinks that excision of the head of the radius would appear to offer the best chances in these cases. Fracture of the coronoid process was not associated.

43. Stimson.[34] A man, aged thirty-six years, fell from a truck with his arm under him. The outer side of the elbow was much swollen. Examination showed the ulna displaced backward about one-half inch and the head of the radius probably fractured. Six weeks later he came under Stimson's care, with the elbow fixed at an angle of above 160 degrees and rotation lost. Operation showed the head broken into several pieces, which were removed. There was also a fracture of the coronoid process. Rotation is now (twelve weeks after the accident) possible for about 20 degrees, and there is enough flexion to suggest that the joint in time will become fairly useful.

44. Stimson.[34] A man fell about twelve feet, striking the ground with the right arm under him. Examination showed the head of the radius to move with the shaft. There was considerable swelling and marked lateral obliquity of the elbow-joint. Stimson thought it a fracture of some part of the external condyle or of the capitellum, and the arm was dressed. Three weeks later all motion of the joint was abolished and the head of the radius was more prominent externally than it should be, although it still moved with the shaft. The elbow-joint was opened on the external aspect, and a fragment, comprising two-thirds of the radial head, found with its articular surface directed outward and backward, but reunited with the shaft. It and the remaining portion of the head of the radius were removed by forceps. Repair was so far advanced that one could not say whether or not the inner portion of the head had also been broken off from the shaft. So far as could be seen through the wound, the coronoid process was uninjured.

45. Latarjet and Gazet.[35] A man, aged twenty-three years, one month before his entrance to the hospital, fell from a tree on his hands. On examining himself he perceived that he could not bend his arm. Examination on admission showed a lateral deviation at the elbow. Flexion and extension of the elbow were limited, pronation and supination were impossible. The ulna was felt to be normal in position. Palpation posteriorly showed the head of the radius to be absent from its normal position, while it could be clearly felt anteriorly. Exeision of the head showed it to be splintered.

46. Latarjet and Gazet.[35] A man, aged twenty-six years, fell seven or eight metres on his right side and could not raise himself. There was some swelling on the external side of the elbow. Spontaneous pain was acute, and impotence complete. Provoked movements were very painful, and it was impossible to supinate the forearm without causing pain. The epitrochlea, epicondyle, and olecranon were in their normal positions and were not painful, but the pain was very acute at the level of the head of the radius, about a finger's breadth below the level of the radial cup. Pressure on the bones of the forearm at their lower ends provokes much pain at this level. Crepitation is distinct, but the head moves on pronation and supination.

47. Banks.[36] A surgical nurse in the Marine Hospital, Chicago, while "skylarking" in the kitchen, stumbled and fell, striking on his left open palm, which he had thrust out

to save himself. He received the full weight of the body on that arm. Examination shortly after the accident revealed crepitus at the joint, the radial head not turning in the complete arc of rotation. Extension and flexion were limited. A tentative diagnosis of fracture of the radial head was made, and was confirmed by the skiagraph. The writer believes the fracture was the result of indirect violence and muscular force. The arm was dressed in semiflexion, between pronation and supination, and passive motion was begun early. An almost perfect result followed. There is complete extension, and only a small portion of the arc of pronation and supination is not capable of its function.

48. Helferich.[37] In his work on fractures and dislocations, Helferich gives an illustration of a deformed head of the radius, the result of union by bone after a fracture. The specimen was obtained by resection from a woman, aged twenty-eight years, who had fallen on the outstretched hand. The joint was stiffened at an obtuse angle, and pronation was limited.

SUMMARY OF THE LITERATURE.

Number. There were 45 patients and 48 fractures, both elbows being involved in 3 cases.

Age. In 36 cases the patients had reached adult life. One was thirteen years old, 1 sixteen, 1 nineteen, and 1 twenty; 6 were dissecting-room or museum specimens, and were without history. Museum specimens without history usually come from the dissecting-room, and as children's bodies rarely find their way into the dissecting-room, they were all probably from adults. That would make a total of 42 adults and 4 adolescents. In 2 cases the age was not given.

Sex. Thirty-four occurred in males, 5 in females, and in 9 the sex was not given.

Causes. There is a history of a fall on the hand in 7 cases, a fall on the elbow in 5, a fall on the forearm in 1, and a fall without mentioning the particular part of the body striking the ground in 15, or 28 giving a history of a fall. In 1 a heavy mass fell on the arm, in another the patient was thrown against machinery, in a third the arm was crushed between the bumpers of cars, and in a fourth a kick of a horse was given as the cause. In 16 the history did not give the cause.

Complications. In 22 cases there were apparently no complications, and in 1 more no complications at the elbow, but serious injuries elsewhere. There were 4 posterior dislocations and 5 compound fractures. There were 9 fractures of the coronoid process, 6 fractures of the external condyle, and probably 2 more.

The following list will show the kind and frequency of the various complications: Posterior dislocation, with fracture of the coronoid process, 2; posterior dislocation alone, 1; posterior dislocation with Colles' fracture, 1; compound fracture of the elbow, with fracture of the coronoid process, 1; compound fracture of the elbow, with suppuration of the joint, 1; compound fracture of the elbow, with fracture of the olecranon and coronoid process, 1; compound fracture of the elbow, with fracture of the external condyle, 2; fracture at the junction of the upper and middle thirds of the radius, 1; fracture of the coronoid process alone, 4; fracture of the olecranon and neck of the radius, 1; fracture of the upper end of the ulna, 1; fracture of the skull, contusion of the brain, and fractures of the humerus and ulna, 1; paralysis of the posterior interosseous nerve, 1; severe rupture of the orbicular ligament, 1; probable crushing of the soft parts, 1; probable fracture of the external condyle, 2; both radii fractured at their lower ends, 1; anterior dislocation of the head of the radius, 1.

Varieties of the Fracture of the Radial Head. The detached fragment was anterior in 6 and external in 7. Its position was not mentioned in 20. In 6 the head was divided into several fragments, and in 2 there was fracture of the neck, with two fragments of the head. Separation of the epiphysis was present in 1, in 5 there was no description of the kind of fracture present, and in 1 there was a forked divergence of the fragments.

Diagnosis. The diagnosis was made by anatomical investigation in 40 cases. It was made during life by crepitus with other signs in 8.

Results. Death from the accident immediately, or very soon afterward, occurred in 11 cases, and in 15 more amputation or excision was done so soon after the accident that there was not sufficient time for complete healing of the fractures. There was good union without deformity of the head in 3 cases, and good union with some deformity in 4 more. In 1 there was perfect function afterward, and, judging from the skiagraph taken at the time of the fracture, there must have been some deformity of the head. In 5 there was non-union, and in 3 more the fragments became movable bodies in the joint, and the fractures, therefore, ununited. In 1 there was bony ankylosis of the elbow, and in another the joint was stiffened at an obtuse angle. In 1 there was impaired function, but a useful limb, and in 3 the results were not mentioned.

CASES SHOWN BY THE SKIAGRAPH, BUT WITHOUT HISTORIES.

Ross and Wilbert[38] (1899) report a series of 500 consecutive cases of fractures of the extremities, as shown by the skiagraph.

Eight were fractures of the head and neck of the radius. There were 5 fractures of the coronoid process, and only 1 of these was associated with fracture of the head of the radius.

The fractures of the head of the radius, as a rule, were not extensive, and in the majority of cases involved the upper and forward part of the articulating surface of the head; 2 were accompanied by fracture of the external condyle.

The same writers[5] (1900) give a second series of 500 cases. There was 1 case of fracture of the head of the radius with fracture of the coronoid process, 5 fractures of the radial head alone, and 2 more accompanied by fracture of the external condyle.

They also[40] (1902) report a third series of 500 cases: 1 was a fracture of the head of the radius with a fracture of the external condyle, and 2 involved the head of the radius alone.

There were 4 fractures of the coronoid process, but it is not shown that any were associated with fracture of the head of the radius.

June 14, 1905, before the Philadelpdia County Medical Society, the writer read a preliminary communication on this subject, in which he dealt chiefly with the question of frequency.

In the discussion which followed, Dr. G. E. Pfahler, of the Medico-Chirurgical Hospital, reported that he had made a search of his collection of skiagraphs, about 500 in all, and had found among them 10 cases of fracture of the head of the radius.

Dr. M. K. Kassabian, of the Philiadelphia Hospital, reported that he had in his collection 8 cases of this fracture. No statement was made of his total number of fractures.

Dr. H. K. Pancoast, of the University Hospital, has kindly made a search of his collection of skiagraphs, and has found 19 fractures of the head and neck of the radius. Of these, 10 were complicated by dislocation or other fractures at the elbow and 9 were uncomplicated. He has been engaged, recently, in counting and classifying his collection, but has not yet completed the task; so that the relative frequency of this fracture, in his experience, cannot be stated at present.

There are, therefore, in the hands of four skiagraphers in Philadelphia, represented by skiagraphs, a greater number of fractures of the head and neck of the radius (55) than the writer could find reported with any attempt at a history or detailed description of the fracture, after a careful search of the literature (48), making a total of 103.

EXPERIMENTAL WORK.

From a study of my own cases and their skiagraphs, and a review of the literature, I concluded that the most frequent cause of this fracture was a fall on the hand with the elbow extended. Bruns[4] had already applied this principle with some success. He disarticulated the upper extremity at the shoulder-joint. With the palm on the ground and the arm in extension, he struck his blows on the top of the humerus. He obtained in all three fractures of the radial head, two incomplete and one complete, the latter splitting off the anterior and outer portion of the head. No further mention is made of his results. I placed the forearm in nearly full pronation—*i. e.*, in the position occupied by it in the usual fall on the hand. In applying the force to the top of the humerus an ordinary wooden mallet (weight one and one-half pounds) was used, and the blows were repeated until the object for which they were applied was accomplished. In two specimens a much heavier instrument (fifteen pounds) was employed.

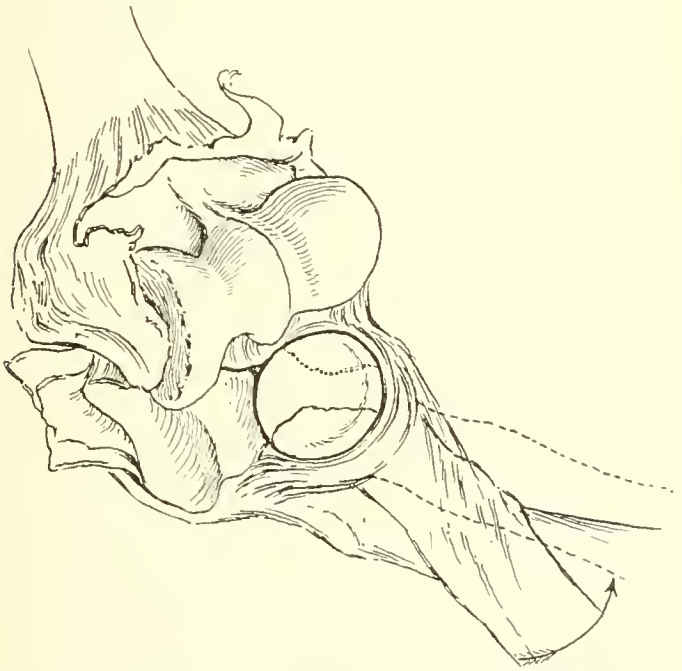

FIG. 1.—The illustration shows some of the more important typical conditions found in the experimental fractures. The dotted lines indicate the positions of the radius and of the fragment, in full or hypersupination; the continuous lines, their positions in full or hyperpronation. The close apposition of the fragments, due to the close-fitting orbicular ligament, and the approximate wedge-shape of the detached fragment are clearly shown.

Owing to the free rotation of the head of the radius, some difficulty is experienced in making clear the position occupied by the detached fragment. The arc of rotation of the head is approximately one of 180 degrees; so that that portion of the head which is posterior in supination is anterior in pronation, etc. Judging from the experimental results, the detached fragment will usually occupy a posteroexternal position in full supination, and hence an anterointernal one in full pronation. This has undoubtedly led to confusion in the literature.

In an effort to overcome this difficulty, the detached fragment will be designated according to the position it would occupy in full supination, since the anterior surface of the radius is anterior in this position of the forearm, the poste-

rior surface posterior, etc. It is very likely, according to this method of describing the position of the fragment, that it is posteroexternal in the great majority of cases; but it must be borne in mind that in pronation, in which position the fracture is most frequently produced, this posteroexternal fragment is approximately anterior, perhaps slightly internal, also.

The frequency of an external fragment, in the cases reported in the literature, is probably due to the fact that, owing to the disturbance within the joint, the forearm cannot be fully supinated, and the frequency of the anterior fragment to the fact that from greater disturbance it cannot be supinated at all.

In every specimen in which the mallet was used the head of the humerus was crushed by it without producing a fracture of the radial head. Four arms were thus tried before proceeding to any change in the method. No signs of fracture at the elbow could be detected through the soft structures, and the joint was opened in each case, but no fracture was present. The ligaments were divided in front by an incision from above downward through the orbicular ligament, except in one case, in which the orbicular ligament was nicked at its upper edge and pushed downward, exposing the radial head. The force required to crush the humeral head by the mallet was not sufficient to produce a fracture below. With the heavier instrument this was not the case.

I now decided to saw off the head of the humerus below the comminuted area, and to apply again the blows of the mallet to the upper end of the humerus. It had been my intention to reapply the saw if the humerus again gave way, and to repeat the process with the mallet and saw, alternately, until an injury to the bone below had been produced, or the whole length of the humerus had crumbled. In only one case was it necessary to again saw the humerus, when the extended position of the elbow was employed, to obtain the desired fracture; and in that instance only one more saw cut was necessary. In every attempt with the limb in extension and pronation, except one, exactly the type of fracture was produced which, from a study of the anatomy of the joint, the literature, and my own cases, I concluded should occur —*i. e.*, a separation of the posteroexternal portion of the head of the radius in supination, which was anterior at the time the fracture was produced. The failure was due to a fracture of the lower ends of the radius and ulna, which made further application of the force useless. All the arms used had been dissected by students without disturbing the joints, except in the one in which an incomplete fracture was produced, and in that one an undissected arm was employed.

Specimen I.—This consisted of an arm in which the elbow had been opened and the orbicular ligament divided. It was taken in order that the effect of the blows could be more easily watched. Many heavy blows (they were not counted) were necessary before the desired result was obtained, and the first sign observed was the posteroexternal third of the radial head, now anterior, separated from the rest by a wide margin, and almost hanging from it. The loose fragment was attached along its lower margin by the reflected fibres of the capsule and the periosteum to the neck of the bone. The head was divided into two nearly equal parts. A very small part of the detached fragment, involving the upper cup-shaped surface of the head, was almost completely separated, only a small part of the cartilage on the upper surface holding it in place. It had no attachment to the reflected capsule or periosteum. Such a fragment might easily become a loose body in the joint later, especially as it was from the upper surface of the head and might pass upward into the free part of the elbow-joint in front.

In full pronation of the forearm the whole detached fragment looked chiefly anterior and slightly internal. The line of fracture on the ulnar side passed through the lesser sigmoid cavity of the ulna. The detached fragment was replaced in its normal position with relation to the rest of the head, and the forearm placed in full supination. The detached fragment now looked about equally external and posterior. It was then grasped by the thumb and index finger through the intact portion of the capsule which now covered it, and a fairly vigorous effort made to produce mobility and crepitus. Both were obtained to a slight degree only. The irregularity in the fractured surfaces, and the pressure toward its fellow necessary in the effort to grasp the small fragment, tended to defeat the purpose. The line of fracture was almost straight, which explains the crepitus and mobility of the fragment in this specimenn.

Specimen II.—In this arm the anterior part of the capsular ligament had been removed down to the level of the orbicular ligament, and this had been stripped downward to expose the circumference of the head, or that portion of it which would pass into view in rotation of the forearm. The limb was placed in position as before, and a fracture produced as in the first specimen. The fragment represented about the posteroexternal third of the head, and, as in the first, looked anteriorly and inward in full pronation and externally and posteriorly in full supination. It was found separated from the rest of the head by a considerable cleft, the orbicular ligament not being in place. The fragment was then replaced in its normal position, and the normal contour of the head reformed. Free and full rotation of the forearm was now carried out without any pressure of the fingers on the fragments, and without the production of any mobility of the fragments or crepitus. The fragments maintained their normal positions without the support of the anterior part of the orbicular ligament. Then the finger and thumb were applied to the circumference of the head, and rotation of the head under them was carried out, first with the orbicular

ligament in place, and afterwards with the finger and thumb applied directly to the head. Though the detached fragment and the remaining portion of the head, with the lines of fracture, passed under the pressing fingers, not the slightest displacement or crepitus was detected. The detached fragment was then grasped between the finger and thumb and a vigorous effort made to move it from side to side on the other fragment. No crepitus or mobility could be produced. The pressure necessary in the efforts to grasp the fragment only forced it more firmly into place, the irregularities of the one fragment fitting the more closely into those of the other. When the detached fragment was drawn forward from its fellow it hung loosely by the thin membranous attachment below, which corresponded to the whole lower border of the fragment. The coronoid process was intact, and no other fracture was present.

Specimen III.—In this arm the capsule of the elbow had not been opened. The same method was used in this as in the other two. The result was a fracture of the radius and ulna just above the wrist. The elbow was examined thoroughly, especially about the head of the radius by direct manipulation, with and without the aid of pronation and supination, flexion and extension, but no evidence of fracture was found. Thinking that the force of the blows of the mallet had been expended in the production of the fracture of the two bones below, I threw the specimen aside to take up another arm. I was not satisfied, however, and again picked it up. I now made very firm pressure on the head with my fingers, while the forearm was rotated with the other hand, and I thought I now detected passing under my fingers such a mark as would be made by the edge of a thin, sharp knife in cartilage. The joint was opened and the divided ligaments stripped aside. I watched the margins of the head as it was rotated, and at first did not detect a line of fracture. Then I found the place which had given to my finger the sensation of a cartilage cut, and a very faint line of separation at this place could be traced downward. What remained of the synovial fluid seemed to have covered over and almost completely obliterated the line of fracture. The finger was then applied to the top of the head and a fragment equivalent to the posteroexternal third of the head in supination was separated, the lines of fracture being vertical as in the other cases. On the upper surface of the head they passed from the margins of the fragment toward the centre of the head, giving the fragment a more or less wedge shape. The same efforts at producing crepitus, mobility, and deformity were applied as in the other specimens, but absolutely failed. Of course, the fragment could be separated from its fellow, grasped by its edges, and then rubbed against the other, but, after being replaced in its normal position, it could not be so taken up by grasping its articular border, and the efforts to do so only forced it more snugly into place. The decided wedge shape made lateral movement impossible. As in the other specimens, the detached fragment in full pronation looked forward and inward, and in full supination outward and backward. There was no other fracture at the elbow.

Here is indisputable evidence that the cause which produces a Colles fracture may also cause a fracture of the head of the radius. It also emphasizes the necessity for great care in the interpretation of the skiagraph wherever there is any reason to suspect this fracture. Again this specimen shows, I believe, that union may occur in some cases in life, even if the normal movements of the joint were performed during the healing process, and little evidence of fracture be left in the bone afterward. I have seen such a specimen of close union without any deformity in the Mutter Museum of the College of Physicians of this city. No reference to fracture of the head is made in the catalogue of the specimens, with reference to this bone.

Specimen IV.—This arm was placed horizontally on the ground, the forearm held vertically, and the hand bent backward. The blows of the mallet were applied to the palm just over the wrist. With much less violence than was used in the previous cases a Colles fracture was produced. The elbow-joint was opened, and a careful examination of the head and neck of the radius made. No fracture was present, nor were any other bones at the elbow injured. In the flexed position of the elbow the whole radial head is in more direct contact with the capitellum of the humerus, and is therefore better protected from injury, since the force of the blow is received by the whole head, and not by a part of it as it falls on the hand in the extended position of the elbow.

Specimen V.—With the palm on the ground the forearm in pronation, but with the elbow flexed to an angle of about 30 degrees, the blows of the mallet were applied to the top of the humerus as before. The head was crushed by a few blows. It was sawed off and the force again applied to the new upper end of the humerus. After many hard blows this gave way, and another saw cut was made below. The mallet was again applied, and again the humerus gave way. Another saw cut was made, this time about three inches above the base of the condyles, and once more the humerus splintered under the blows of the mallet. The elbow was then examined for fracture first before opening the joint, and then more thoroughly after opening the capsule in front. No injury to the bones could be found.

Von Bergmann[39] says that the fracture occurs in falls on the hand when the forearm is moderately flexed and pronated. This specimen would tend to disprove that statement, especially in view of the fact that the fracture was so easily and constantly produced in extension.

Since the head of the radius is more completely in contact with the capitellum in flexion, I had hoped, by maintaining

the limb in this position and applying the heaviest blows that I could wield, to produce a multiple fracture of the head, or a fracture of the neck, instead of separating only the posteroexternal part of the head.

Specimen VI.—With the palm on the ground and the limb in the extended, pronated position, the blows of the mallet were applied to the top of the humerus. This gave way, and was sawed off below the surgical neck. Again the blows broke the upper end of the humerus, which was sawed off lower down. I had learned by this time to detect a certain sensation which indicated a loss of resistance at the elbow, and which in the previous experiments proved to be due to a fracture of the head of the radius. This sensation was now present, and upon palpating the head through the unopened capsule I thought I felt a line of fracture passing under my finger during rotation. Neither mobility of the fragment nor crepitus could be produced after persistent trials, both by rotation of the head under the fingers and by direct manipulation. Again the limb was placed in position, and a persistent hammering kept up for some time. I desired to separate the fragments freely by continuing to drive the capitellum against the detached fragment. The only progress made was shown in a more easy recognition of the lines of fracture, and the presence of slight crepitus, both on rotation and direct manipulation, but no more by the one method than by the other. Again the limb was placed in position and the blows of the mallet applied. Although these were far more numerous than before and the hardest that I could deliver, practically no progress was made. It is evident, from a study of the anatomy of the part, that the detached fragment was the only bony support on the radial side of the joint. Therefore, from lack of resistance, the humerus should descend on that side, if the force were strong enough, driving the detached fragment before it. I had hoped in this way to force the fragment downward and forward against the orbicular ligament, thus bursting it and producing a specimen in which the fragment would be freely movable. When the fracture of the head of the radius occurs from only moderate force, as in these experiments, the ulna seems to be strong enough to prevent further damage. Upon opening the joint a small splinter from the ulnar side of the coronoid process was found, still strongly attached by ligamentous material. It could scarcely be called a fracture of the coronoid process. We have here an explanation of why the orbicular ligament is not more frequently lacerated, and the fragments more widely separated.

The detached fragment of the radial head represented slightly more than the posteroexternal third. Like the others, it was attached to the reflected capsule and periosteum, and held the same position relative to pronation and supination. It was also wedge-shaped, but the angle was more obtuse than in some of the others. This and the more than usual loosening of the fragment explain the slight crepitus detected.

Specimen VII.—The palm was placed on the ground, the forearm pronated, and the elbow flexed to a right angle. As flexion was the position in which the head was fully in contact with the capitellum, and I had failed to comminute the head by other flexed positions, I concluded to try this and to strike over the condyles. The resistance to the blows was decidedly less marked than in the extended position, and I feared that the condyles would give way before a fracture of the head could be produced. Although they withstood much better than had been expected, they finally broke and, upon clearing away the soft tissues, a T-fracture of the humerus was disclosed, but no fracture of the radius or ulna.

Specimen VIII.—An undissected limb was placed in the extended and pronated position with the palm on the ground. The head of the humerus withstood unusually well, but finally broke, without evidence of injury at the elbow. The head was sawed off and the mallet applied vigorously and for a long time. The bone in this case seemed to be unusually resisting. After what seemed to me several times the force usually necessary to produce the fracture of the head of the radius, I failed to detect any sign of fracture at the elbow. The joint was then opened by an incision from the upper part of the elbow downward over the head of the radius to its neck. I do not recall the position of the forearm at this time, but I believe that it was in supination. The border of the head was examined closely, as it was rotated, and all that could be found was a very fine vertical mark in the most prominent part of the circumference of the head. It was about one-eighth of an inch long, and did not extend to the rounded edge of the cup above, nor to that of the border below. I concluded at first that it had been made by the knife in opening the joint. The limb was again placed in position, and many hard blows applied as before. The border of the radial head was examined again in all positions. The only sign of a fracture that could be seen was a slight increase of the small fissure, which I had observed before. It was evidently a break, and I now worked into it the point of one blade of an ordinary dissecting forceps, which increased it slightly. The external lateral ligament was then divided to expose the upper surface of the head. A very faint fissure, continuous with that on the vertical border, could be traced almost to the centre of the cup. (See Fig. 2.) On the circumference it passed only to the lower border of the expanded portion of the head. This was the first incomplete fracture that I had obtained, and it was evidently due to the greater resistance of the bone in this specimen. In addition to the main fissure, and just to its radial side, could be seen two very small ones, parallel to each other, and almost parallel to the main fissure. After placing the limb again in position and striking it very vigorously with the mallet, I took hold

of the border of the head on the outer side of the main fissure and pressed downward. This portion yielded in such a way as to show that if the blows were continued about the anterior third of the head would have been separated. As this was the only specimen of an incomplete fracture that had been produced, I concluded to keep it.

Specimen IX.—Instead of using the wooden mallet I now selected a heavy iron instrument for striking the humerus. It weighed fifteen pounds. The limb was placed in the extended pronated position as before, and a heavy blow struck on the top of the humerus. At once there was produced a fracture of the lower ends of the radius and ulna. The head of the radius was carefully examined, first through the unopened capsule, and then by direct exposure of the bone. No fracture was present. This was the first time I had failed to produce the fracture of the head in this position. I did not try again with this specimen because of the fracture below. The head of the humerus was slightly dented by the blow, but was not broken.

Specimen X.—I had observed that when striking on the top of the humerus with the limb in extension, even with the mallet, the elbow bent slightly every time the blow was received. In the last experiment the flexion from the heavy blow was so violent that an unpleasant strain was exerted on the hand which was holding the limb in position. In this case I placed the limb in position against a heavy box and fastened it with nails. Several blows, not quite as heavy as in the last case, were then struck on the top of the humerus. The result was a fracture of the posteroexternal third of the radial head. Again the head of the humerus was slightly flattened by the blows, but not broken. A careful examination of the head of the radius through the unopened capsule failed to disclose a fracture, which was evident on opening the joint. After pulling the small fragment away from its fellow, and again putting it in position, very slight crepitus and mobility could be obtained. The line of fracture was about straight, not wedge-shaped. With the fragments in close apposition, the capsule was sewed tightly over them. The mobility and crepitus could still be elicited. With such a line of fracture one cannot fit as easily or as nicely one

Fig. 2.—This is an illustration of the experimental incomplete fracture produced by the writer. It shows the main fissure on the ulnar side of the head, which does not reach the neck of the bone, and the two smaller and parallel fissures toward its radial side. By their position and direction they divide the head into a larger or posterior portion in pronation and an anterior or smaller portion. The anterior part represents the posteroexternal part of the head, and yielded to downward pressure of the finger, showing that it would have been a complete fracture if the force had been strong enough.

fragment to the other as when the fragment is wedge-shaped. This, I believe, explains why crepitus was obtained after the fragments had been separated and replaced in position.

(To be continued.)

THE BACTERIA ENCOUNTERED IN SUPPURATIONS.

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For a number of years in the microscopic and bacteriological study of pus from different sources, I have been surprised at the frequency with which bacteria are encountered that are not usually classed as having pyogenic properties. In obtaining material for class demonstrations it is not always possible to obtain specimens that are desirable in every way, because it is not always possible to secure cases with typical abscesses from which to obtain pus for these demonstrations. In place of such characterisitc material it has frequently been necessary to employ the discharges from a variety of suppurating wounds, and it is especially in the pus derived from these sources that the organisms to which I refer have been encountered.

With the foregoing results in mind, I thought it might be of interest to take a series of specimens of pus obtained from cases in the hospital, of the character described, and ascertain what bacteria could be found. I have taken a series of 30 cases without any selection, simply availing myself of the opportunity of examining pus, whatever the source may have been. The cases examined included 6 that were diagnosed as being tuberculous; 4 were abscesses of the inguinal and rectal region; 2 were cases of empyema; 1 carcinoma of the breast; several superficial ulcers, and the remainder were either suppurating wounds or cases in which suppuration followed various operative procedures. In 24 of the 30 cases staphylococci were encountered, either alone or in conjunction with other organisms. Streptococci were found six times. Bacillus pyocyaneus was found in 9 cases. In 4 of the cases bacillus coli was encountered. Aside from these organisms bacillus vulgaris was encountered several times; bacillus alkiligenes was encountered once, and several bacilli the exact identity of which I have not definitely determined. And in 13 of the cases an organism having morphological characters simulating those of bacterium diphtheriæ was encountered.

The frequency with which bacterium pseudodiphtheriticum had previously been encountered in routine examinations of pus led me to believe that in certain suppurating conditions this organism might be concerned in contributing toward the general effect, and I was not at all surprised at the frequency with which I encountered organisms like bacterium pseudodiphtheriticum, namely, in 13 different cases, or 43.3 per cent. of the cases examined. In many of the specimens of pus bacterium pseudodiphtheriticum was present in very large numbers, far exceeding in number all the other bacteria.

Table I.—Cases in the Surgical Wards, University of Pennsylvania Hospital, from which specimens of pus were obtained.

Number.	Staphylococci.	Streptococci.	Pseudomonas aeruginosa.	B. pseudodiphtheriticum	B. coli.	Name of patient	Disease.
1	Aureus	...	...	+	+	John McC.	Tuberculous abscess.
2	.....	...	+	+	...	Peter K.	Compound fracture of fibula.
3	Aureus	...	...	...	...	Alex. M.	Halsted plate operation.
4	Aureus	...	...	...	..	Thomas P.	Ulcer—varicose veins.
5	Aureus	...		+	...	Maggie C.	Carcinoma of breast.
6	.....	...	...		...	Reana M.	Tuberculous glands of neck.
7	Aureus	...	...	...	...	John G.	Tuberculous knee-joint.
8	Aureus	...	+	...	...	John E.	Chronic osteomyelitis.
9	Albus aureus	+	...	...	...	Maude G.	Tuberculous hip.
10	Albus aureus	+	+	...	...	David M.	Tuberculous hip.
11	Albus aureus	...	...	+	...	Gertrude M.	Inguinal abscess.
12	.....	...	+	...	...	Frank C.	Empyema.
13	.....	+	...	...	+	Mary McC.	Rectal abscess.
14	Aureus	...	...	...	...	Blanche Z.	Empyema.
15	Albus	...	...	...	...	Mary N.	Specific ulcer, shoulder.
16	Aureus	...	+	...	+	Clayton W.	Iliac abscess.
17	Aureus	...	...	+	+	Mr. C.	Osteomyelitis.
18	Citreus	...	...	...	...	D. C. G.	Psoas abscess.
19	Albus aureus	...	...	+	...	Mr. E.	Contused and lacerated wound.
20	Aureus	+	...	+	...	John S.	Sarcoma—eye.
21	Aureus	...	...	...	...	Mary W.	Empyema.
22	Albus aureus	...	+	...	...	Jeremiah R.	Inguinal hernia.
23	Albus aureus	...	...	...	...	William P.	Amputation of leg.
24	Aureus	...	...	+	...	Thomas C.	Gangrene following dislocation.
25	.....	...	+	...	...	Sylvester C.	Tuberculous hip.
26	.....	...	...	...	...	?	Operation for gallstones.
27	Citreus aureus	+	...	+	...	Rosaria C.	Superficial gangrene of thigh.
28	Aureus	...	...	+	...	John K.	Amputation of hand.
29	Aureus	...	...	+	...	Mrs. B	Appendicitis.
30	Aureus	+	...	+	...	Anna P.	Osteomyelitis.

As long ago as 1898 ("Contributions from the Laboratory of Hygiene," University of Pennsylvania, 1898) I called attention to the fact that I had discovered organisms of the pseudodiphtheriæ group in superficial suppurating wounds. The mild degree of pathogenic power which I was able to demonstrate in the organisms of this group at that time did not seem to indicate that they were organisms of great moment in such conditions. However, the frequency with which I have since encountered these organisms in pus, and the frequency with which I encountered organisms of this type in cows' milk, where there was apparently a chronic catarrhal condition of the milk sinuses (*Journal of Medical Research*, May, 1904, vol. xi.), and, moreover, the fact that I had encountered organisms of this type in typical abscesses occurring spontaneously in mice in this laboratory, led me to take up the systematic study of these organisms.

In the light of my experience in the investigations in 1898, where, in several instances, undoubted purulent effects were demonstrated in the intraperitoneal injection into guinea-pigs, I attempted to increase the pathogenic powers of these

bacteria by repeated injections into the peritoneal cavities of guinea-pigs. The operation requires considerable time in order to bring about positive effects, but I have succeeded in bringing several of my cultures to a point where they produce purulent conditions in the peritoneal cavity of the guinea-pig, attended frequently by fatal results. So far it has not been possible to kill the animals with less than two or three cubic centimetres of a twenty-four-hour bouillon culture. When death follows the intraperitoneal injection of the culture it usually takes place in eighteen to thirty-six hours, and is accompanied with interesting results. There is sometimes a marked subcutaneous œdema similar to that seen in inoculations of bacterium diphtheriæ, but with only slight local hyperæmia at the point of needle puncture. The peritoneal cavity always contains some fluid, which contains a great many cells. The adrenals usually present a definite hyperæmia, though this is rarely as marked as in infection with bacterium diphtheriæ. In a general way the lesions are frequently quite similar to those produced by inoculations of bacterium diphtheriæ. In the animals dying within eighteen to thirty-six hours after inoculation the inflammatory reaction in the peritoneum is not very marked, though when death is delayed there is considerable evidence of inflammation.

The cellular elements found in the peritoneal fluid are very interesting. If an animal is injected with a non-fatal dose of the organisms and killed forty-eight hours subsequently, most, if not all, of the organisms are found to have been taken up by the large numbers of polynuclear leukocytes which are present. The fluid also contains small amounts of erythrocytes and small and large mononuclear leukocytes and endothelial cells. The phagocytic activities of the endothelial cells are most interesting, as frequently they are seen to have taken up not only the erythrocytes and the other cellular elements, but especially the phagocytic polynuclear leukocytes. It is not unusual to see in one of these large phagocytic endothelial cells one or more erythrocytes as well as several polynuclear leukocytes that are packed with the bacteria. It is evident from these facts that there are two important agents in removing these bacteria from the body.

If an animal is inoculated with a fatal dose of a virulent culture the picture in the peritoneal fluid, postmortem, is quite different. A great many polynuclear leukocytes are found, but relatively few that have manifested their phagocytic powers, as practically all the bacteria are extracellular. The number of endothelial cells and mononuclear leukocytes is usually less than in the injection of non-fatal doses.

The repeated intraperitoneal inoculation of guinea-pigs has shown that it is possible to increase the aggressive or invasive powers of these bacteria to such an extent that they bring about acute septic peritonitis. At no time was a general invasion of the body encountered. The bacteria were always localized in the peritoneal cavity of the animal. In subcutaneous injections a local abscess was developed from which the animal recovered. The limited phagocytosis, seen postmortem, indicates that the agressive power of the bacteria is manifested through inhibition of the phagocytic powers of the polynuclear leukocytes. Aside from this it appears probable that the toxic powers of the bacteria have become augmented, especially so from the presence of subcutaneous œdema and hyperæmia, and hyperæmia of the adrenals.

The fact that bacterium pseudodiphtheriticum was always found in association with the more common pyogenic bacteria indicates that it is probably not the primary cause of the suppuration; at least, in the cases examined.

TABLE II.—Cases from which Bacterium pseudodiphtheriticum was isolated.

No.	Name.	Disease.	Other bacteria also found.
1.	Reana M.	Tuberculous glands of neck.	
2.	John McC.	Tuberculous abscess.	Bacillus coli, Staphylococcus aureus.
3.	Gertrude M.	Inguinal abscess.	Staphylococcus albus, Staphylococcus aureus.
4.	Mr. C.	Osteomyelitis.	Bacillus coli, Staphylococcus aureus.
5.	Mr. E.	Contused and lacerated wound.	Staphylococcus albus, Staphylococcus aureus.
6.	Peter K.	Compound fracture of fibula.	Pseudomonas aeruginosa, Staphylococcus aureus.
7.	John S.	Infected eye cavity.	Staphylococcus aureus, Streptococcus pyogenes.
8.	Maggie C.	Carcinoma of breast.	Staphylococcus aureus, Pseudomonas aeruginosa.
9.	Thomas C.	Gangrene following amputation of leg.	Staphylococcus aureus.
10.	Rosaria C.	Superficial gangrene of thigh.	Staphylococcus citreus, Staphylococcus aureus, Streptococcus pyogenes.
11.	John K.	Amputation of hand following gunshot wound.	Staphylococcus aureus.
12	Mrs. B.	Appendicitis.	Staphylococcus aureus.
13.	Anna B.	Osteomyelitis.	Staphylococcus aureus, Streptococcus pyogenes.

The cases in which bacterium pseudodiphtheriticum was found represent cases with both acute and chronic lesions, though the latter predominate. This fact leads to the supposition that these bacteria are concerned more in maintaining the suppuration than in originating it, though in Case V (Table II.) they were present in large numbers soon after the injury had been received. The same is true of the case of gangrene (Case IX.).

Sproneck (*Deutsche med. Wochenschr.*, 1896, p. 571) found that quite a large number of cultures of bacterium pseudodiphtheriticum are capable of producing infiltration at the point of inoculation. Levy and Fickler (*Deutsche med. Wochenschr.*, 1900, p. 418) isolated bacterium pseudodiptheriticum from vaccine which was pathogenic for rabbits, guinea-pigs, and white mice. Kruse and Pasquale (*Zeitschr. f. Hygiene*, 1894, Bd. xvi.) isolated an organism of this group from a liver abscess in dysentery. Recently Ruedinger and Hamilton (*Journal of Infectious Diseases*, 1904, p. 690)

found organisms of this group that possessed undoubted pathogenic effects in man as well as in laboratory animals.

The occurrence of bacterium pseudodiphtheriticum in vaccine virus as well as in the lesions of smallpox has long been known. The relation of these bacteria to such lesions is no doubt explainable on the same basis as the occurrence of staphylococci and of streptococci under similar conditions. Bacterium pseudodiphtheriticum, like the staphylococci and streptococci, is found almost constantly on skin and mucous membranes of man and the domestic animals, and hence gains access to wounds and abrasions in the same manner as do the common pyogenic bacteria.

In the light of the results of this investigation and the numerous observations on the occurrence and activities of bacterium pseudodiphtheriticum, we must regard these bacteria, at least some of the varieties, as being pyogenic organisms.

Another interesting phase of the investigation is the variation noticed in the cultures of pseudomonas aëruginosa isolated from the different cases.

Table III. shows the nature of the cases from which this organism was isolated, as well as the other bacteria also present.

Table III.—Cases from which Pseudomonas aëruginosa was isolated.

No.	Name.	Disease.	Other bacteria found.
1.	Peter K.	Compound fracture of fibula.	Bacterium pseudodiphtheriticum,
2.	Maggie C.	Carcinoma of breast.	Staphylococcus aureus, Bacterium pseudodiphtheriticum.
3.	John McC.	Tuberculous abscess.	Staphylococcus aureus, Bacterium pseudodiphtheriticum, Bacillus coli.
4.	Frank C.	Empyema.	
5.	David M.	Tuberculous hip.	Staphylococcus aureus and albus, Streptococcus pyogenes, Bacillus proteus.
6.	John E.	Osteomyelitis.	Staphylococcus aureus and albus.
7.	Mr. E.	Contused and lacerated wound.	Staphylococcus aureus and albus, Bacterium pseudodiphtheriticum.
8.	Sylvester C.	Tuberculous hip.	Bacillus proteus.
9.	?	Operation for gallstones.	

As will be seen from the details given in Table III., pseudomonas aëruginosa was encountered in 9 of the 30 cases examined. The nature of the cases from which this organism was isolated is quite various, so that the character of the lesions does not seem to influence the presence of this organism. The interesting part about the cultures isolated from the different cases is the marked variation with regard to their pigment production. The organisms from the different cases were cultivated for a considerable period of time on different culture media in order to establish some uniformity in their chromogenic properties, without, however, obtaining any satisfactory results. These cultures differed in two particulars: first, with the extent to which they formed bacterial fluorescein; and, second, the extent to which they formed pyocyanin. Seven of the organisms produced fairly large quantities of both pigments; so that there was no difficulty in isolating the blue pigment by means of chloroform. One of the cultures produced a very marked amount of the fluorescein and only traces of the pyocyanin, while another culture formed very small quantities of pyocyanin and the merest trace of the fluorescein; so that from these studies it seems probable that there are at least three distinct types of pseudomonas aëruginosa. Long-continued cultivation on artificial media failed to alter these characters in any particular.

Conclusions.—The results of the investigation indicate that aside from the usually recognized pyogenic organisms—namely, the staphylococci, streptococci, and pseudomonas aëruginosa—a very large proportion of suppurations contain, in addition to one or more of these organisms, bacterium pseudodiphtheriticum.

The experiments and observations made thus far with bacterium pseudodiphtheriticum indicate that it has distinct though rather mild pyogenic properties. The results of the investigation indicate that it is incapable of producing a soluble toxin, but, on the other hand, like the staphylococci and streptococci, it produces an endotoxin.

THE VOLUME OF NITROGEN EVOLVED FROM URIC ACID BY THE ACTION OF ALKALINE SODIUM HYPOBROMITE SOLUTION.

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and

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The absence of uniformity in the volume of nitrogen evolved from the same weight of urea when acted upon under the same conditions by an alkaline solution of sodium hypobromite, as recently described by us,[1] led us to investigate the behavior of an alkaline sodium hypobromite solution with respect to the uniformity of the volume of nitrogen evolved from the same weight of uric acid under the same conditions.

Erdmann,[2] using calcium hypochlorite as the decomposing agent, found that uric acid was only partly decomposed with the evolution of nitrogen and that the amount decomposed seldom exceeded one-half of the ammonia-free uric acid employed. In other cases far less than one-half of the uric acid was decomposed. König, his assistant, using 0.3105 grm. of uric acid and decomposing it with calcium hypochlorite obtained 40.5 c.c. instead of 74.5 c.c. of nitrogen, and in another experiment, using 0.795 grm. of uric acid, obtained only 35 c.c. instead of 216.7 c.c. of nitrogen. Converting these numbers into percentages by volume of the theoretical volume of nitrogen, we have, respectively, 54.3 and 11.5 per cent. Erdmann considered that the concentration of the solution and the temperature appeared to influence the results.

Knop and Wolf,[3] using a strongly alkaline solution of sodium hypochlorite as the decomposing agent, found that uric acid yielded practically one-third of its nitrogen (by weight) as gas when during the process of the experiment the hypochlorite solution was not heated beyond 50° to 60° C. They obtained volumes corresponding to from 11 to 12.6 per cent. by weight of nitrogen, which numbers practically agree with one-third of the theoretical percentage by weight (33.3 per cent.) of nitrogen in uric acid. Converting these numbers into percentages by volume of the theoretical volume of nitrogen, we have, respectively, 33 and 37.8 per cent. Efforts made by them to decompose the uric acid to obtain the theoretical quantity of nitrogen were unsuccessful. However, these investigators suggested that "as the nitrogen evolved is constant in volume, there is a possibility by this method of decomposition of arriving at a conclusion regarding the constitution of the acid."

Hüfner,[4] in two quantitative determinations, using in one experiment 0.0588 grm. and in the other 0.0662 grm. of dry uric acid and permitting the hypobromite solution to act a long time upon the uric acid, obtained, respectively, 46.4 per cent. and 47.4 per cent. of the theoretical volume of nitrogen.

Falck,[5] in two experiments, using 0.1105 grm. and in the other 0.1033 grm. of uric acid, obtained, respectively, 47.92 per cent. and 47.63 per cent. of the theoretical volume of nitrogen.

Summarizing these results, we have the following as the percentages of the theoretical volume obtained: König, 54.3 and 11.5 per cent.; Knop and Wolf, 33 and 37.8 per cent.; Hüfner, 46.4 and 47.4 per cent.; Falck, 47.92 and 47.63 per cent.

Our experiments were made with uric acid obtained from human urine by adding 10 c.c. of concentrated hydrochloric acid to each 200 c.c. of the filtered urine and allowing the liquid to stand until crystals of uric acid separated. These crystals, which were brownish in color, were collected on a filter and washed several times with water. They were then dissolved in an adequate quantity of potassium hydroxide solution and the resulting potassium urate precipitated therefrom by the addition of a large quantity of alcohol. In this manner, by a repetition of the procedure of removing the separated potassium urate by filtering and redissolving in water and reprecipitating with alcohol, a product was obtained which, on being dissolved in water and being treated with hydrochloric acid, yielded a colorless precipitate of uric acid. This precipitate was collected on a hardened filter, washed with cold water until free from chlorine, and, after being dried, was used in preparing the solutions used in the experiments. On igniting a portion of the acid on platinum foil, no residue remained.

The solution of uric acid used was a 1 per cent. solution. It was freshly prepared for each series of experiments by placing 0.250 grm. of dry uric acid, prepared as before described, in a thin-necked, graduated flask of 25 c.c. capacity, and introducing distilled water to the extent of about two-thirds

of the capacity of the flask. Very small pieces of solid potassium hydroxide were added at intervals, to convert the uric acid into soluble potassium urate, until, on the addition of a final portion, the uric acid had completely dissolved. The solution was then diluted to the 25 c.c. mark by the addition of distilled water. The solution was then poured into a small beaker and then back into the flask, and again into the beaker and stirred to ensure thorough mixing.

The hypobromite solution employed was prepared according to the directions of Knop by dissolving 100 grm. of sodium hydroxide in 250 c.c. of water, allowing the solution to cool and then slowly adding 25 c.c. of bromine, at the same time keeping the liquid cool by holding the glass cylinder in which it was contained under a stream of cold water. The solution thus prepared was immediately filtered through asbestos, and in every case used in the Hüfner apparatus within one hour of its preparation. No portions were used a second time. The apparatus used was the one devised by Hüfner. The capacity of the receptacle for the uric acid solution (including the aperture in the cock) of one of the apparatus was 6.1 c.c., and the receptacle for the hypobromite solution 105 c.c.; the capacities of the receptacles in a second apparatus were, respectively, 5.36 c.c. and 100 c.c., and of a third apparatus, respectively, 5.21 c.c. and 112 c.c.

In every experiment the receptacle for the uric acid solution was filled with that solution by means of a long thistle tube, and after each experiment the entire apparatus was rinsed in turn with portions of water, alcohol, and ether before beginning the next experiment. After the removal of the thistle tube the cock was turned and the excess of solution in the upper receptacle was poured out and the receptacle was thoroughly washed with distilled water. After attaching the saucer-like part of the apparatus, hypobromite solution was poured into the upper bulbed receptacle by means of a thistle tube, in order to avoid the production of bubbles of air, and the saucer-like receptacle was nearly filled with distilled water. The tube, graduated in tenths of a cubic centimetre, was filled with hypobromite solution and inverted over the exit tube of the apparatus. To avoid the production of gas, when inverting the graduated tube, by the action of the hypobromite upon the skin of the thumb, the latter in each experiment was coated with a thin film of petrolatum. The cock was then suddenly turned and the decomposition allowed to proceed. The vigorous evolution of gas when hypobromite solution of full strength was used ceased after two and one-half to three minutes. The graduated tube was then removed and suspended in distilled water to await measurement. Immediately after the removal of the graduated tube from the Hüfner apparatus another tube was inverted over the Hüfner apparatus and allowed to remain during periods of time, varying with the experiments, to collect gas that might be gradually evolved after the expiration of the first three minutes, during which the vigorous evolution of gas occurred. The gas evolved during this time was measured separately and its composition determined by means of an alkaline solution of pyrogallol.

In these experiments one of us (Ryan) prepared the uric acid and the solutions of definite strength of the same, also the hypobromite solutions, and made the mathematical calculations; the other (Marshall) performed the experiments with the Hüfner apparatus, transferred the resulting gas, and made the absorptions and readings of volumes of the gas.

The following table shows the volumes of gas obtained in using a 1 per cent. solution of uric acid after two and one-half to three minutes' action of full strength, freshly prepared, alkaline hypobromite solution:

TABLE I.—NITROGEN EVOLVED IN 2½ TO 3 MINUTES.

Experiment.	Vol. of uric acid sol. (capacity of bulb of Hüfner's apparatus).	Percentage of uric acid in solution.	Strength of hypobromite solution.	Vol. of nitrogen obtained in 2½ to 3 minutes.	Temperature, C.	Barometer in mm.	Corrected vol. of nitrogen.	Nitrogen yielded by 1 grm. uric acid.	Percentage of the theoretical vol. of nitrogen obtained.
	c.c.	per ct.		c.c.			c.c.	c.c.	
1	5.36	1	Full strength	3.6	23°	772	3.28	61.19	22.87
2	6.1	1	"	3.8	23	772	3.46	56.72	21.20
3	5.21	1	"	5.4	23	772	4.81	92.32	24.51
4	5.36	1	"	3.3	24.5	763	2.91	54.85	22.00
5	6.1	1	"	4.4	24.5	763	3.93	64.42	24.08
6	5.21	1	"	4.0	24.5	763	3.57	68.52	25.62
7	5.36	1	"	3.7	24	760	3.30	61.50	22.99
8	6.1	1	"	3.8	24	760	3.39	55.70	20.82
9	5.21	1	"	3.0	24	760	2.67	51.24	19.15
							Aver'ge	62.94	23.69

It will be observed that only in two of the nine experiments was there more than one-fourth of the theoretical percentage by volume of nitrogen obtained. The maximum percentage of the theoretical volume obtained was 34.51 and the minimum 19.15. But these observations were based upon the assumption that complete decomposition of the uric acid had occurred after the cessation of the vigorous evolution of gas which, in point of time, required from two and one-half to three minutes. After these periods of time it was observed that at intervals a very small bubble of gas would be produced and ascend through the liquid. These bubbles were collected by placing another tube over the exit part of the Hüfner apparatus. The evolved gas was measured and then treated with alkaline pyrogallol solution to absorb oxygen and the residual nitrogen was measured.

In the following table, experiments numbered 4, 5, 6, 7, 9 correspond to the experiments having the same numbers in Table 1. In other words, they are a continuation of the experiments after the lapse of from two and one-half to three minutes:

TABLE II.—NITROGEN EVOLVED ON FURTHER STANDING.

Experiment.	Vol. of uric acid sol. (capacity of bulb of Hüfner's apparatus).	Percentage of uric acid in solution.	Strength of hypobromite solution.	Vol. of nitrogen obtained on further standing.	Temperature, C.	Barometer in mm.	Corrected vol. of nitrogen.	Corrected vol. of nitrogen after absorption of oxygen with alkaline pyrogallol.	Volume of oxygen absorbed.	Nitrogen yielded by 1 grm. of uric acid.	Percent. of the theoretical vol. of nitrogen obtained
	c.c.	pr.ct.		c.c.			c.c.	c.c.	c.c.	c.c.	
4	5.36	1	Full strength	7.6 (43 hrs.)	26.5	761	6.7	5.29	1.41	96.82	36.90
5	6.1	1	"	10.1 (43 hrs.)	26.5	761	8.97	5.73	3.24	93.93	35.21
6	5.21	1	"	9.4 (43 hrs.)	26.5	761	8.289	5.379	2.91	103.24	38.75
7	5.36	1	"	9.0 (168 hrs.)	24.0	765	6.72	4.29	2.43	80.03	29.92
9	5.21	1	"	10.0 (168 hrs.)	24.0	765	7.47	4.65	2.82	89.25	33.37
									Aver.	92.65	34.83

The results exhibited in this table (II.) demonstrate that after the first vigorous evolution of gas has ceased, the time required being from two and one-half to three minutes, a very slow evolution of nitrogen occurs, and that the volume thus evolved in from forty-three to one hundred and sixty-eight hours averages 34.83 per cent. of the theoretical volume. It appears that evolution of gas is complete after the expiration of at most forty-three hours.

Table III. is a summation of the results exhibited in Tables I. and II.

Thus, as shown in the table, if the percentage of the theoretical volume of nitrogen obtained in two and one-half to three minutes be added to the volume obtained in the same experiment on standing forty-three to one hundred and sixty-eight hours, an average of 57.58 per cent. of the theoretical volume is obtained. Here the maximum percentage of the theoretical volume is shown as 64.37 and the minimum 52.52.

The experiments demonstrate that neither in two and one-half to three minutes nor in from forty-three to one hundred and sixty-eight hours is the theoretical percentage of nitrogen evolved, and, further, that even under the same conditions there is an absence in uniformity of the percentage volumes evolved.

TABLE III.—SUMMATION OF NITROGEN EVOLVED IN 2½ TO 3 MINUTES AND ON FURTHER STANDING.

Experiment.	Vol. of nitrogen evolved by 1 grm. uric acid in 2½ to 3 min.	Percentage of theoretical vol. of nitrogen in 2½ to 3 minutes.	Vol. of nitrogen obtained on further standing	Percentage of theoretical vol. of nitrogen on further standing.	Summation of nitrogen evolved in 2½ to 3 minutes and on further standing.	Summation of percent. of the theoretical vol. of nitrogen in 2½ to 3 minutes and on further standing.
4	54.85 c.c.	22.0	96.82 c.c. (43 hours)	36.9	151.67 c.c.	58.90
5	64.42	24.08	93.93 (43 hours)	35.12	158.35	59.20
6	68.52	25.62	103.24 (43 hours)	38.75	171.76	64.37
7	61.5	22.99	80.03 (168 hours)	29.92	141.80	52.91
9	51.24	19.15	89.25 (168 hours)	33.37	140.49	52.52
				Average	151.81	57.58

Of the investigators mentioned in the beginning of this article, Falck is the only one who, in the two experiments he made, obtained results fairly in agreement with each other. The length of time that the hypobromite is permitted to act upon the uric acid is an important factor, but no mention of a definite time is made by any of the investigators mentioned. Then, too, the fact that oxygen is given off in the experiment, especially if the experiment be prolonged, is not taken into consideration by them.

It is plain that the method is not of quantitative value.

BIBLIOGRAPHY.

1. Ryan and Marshall. UNIV. OF PENNSYLVANIA MED. BULL., Feb., 1905.
2. Erdmann. Journ. f. Prakt. Chem., 1857, vol. lxxi. p. 211.
3. Knop and Wolf. Chem. CentralBl., 1860, p. 263.
4. Hüfner. Journ. f. Prakt. Chem., 1871, N. F., 3, p. 21.
5. Falck. Arch. f. d. ges. Physiol., vol. xxvi. p. 406.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
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This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

HISTOLOGICAL CHANGES ENCOUNTERED IN THE THYMUS AND ELSEWHERE IN A CASE OF CONGENITAL HYPOTONIA.

By Allen J. Smith, M.D.

(From the McManes Pathological Laboratory, University of Pennsylvania.)

In a recent number of the University of Pennsylvania Bulletin (January, 1905), Dr. William G. Spiller, after a brief review of our knowledge of the condition known as *myotonia congenita*, has given the clinical features and results of histological study of central and peripheral nervous structures and muscles presented by a case under his charge in the University of Pennsylvania Hospital, adding thereto a *résumé* of the general findings at autopsy conducted by Dr. A. F. Coca. At the time of publication of Dr. Spiller's article the histological study of the visceral specimens obtained at the postmortem examination had not been reached in the general laboratory, and, unfortunately, no note of the conditions discovered shortly afterward was had by him. With a view of adding what are possibly important data in relation to the affection, the following additional features are offered supplementary to the studies outlined in Dr. Spiller's article upon the case in hand, the first thus far definitely known to have come to the autopsy table.

While not excluding a possibility of the existence of the point of departure in the central nervous system (more particularly the anterior spinal horns) Oppenheim[1] inclines to regard the affection as rather one of the muscular system, resulting in arrest of muscular development; a conclusion supported by Spiller,[2] who has failed to discover in the brain, cord, optic nerves, and peripheral nerves from both upper and lower extremities any gross or minute change, but who notes in muscular tissue taken from the sole of the foot, from the calf of the leg, and from the back of the trunk that the fibres are hyaloid, their transverse striæ well preserved, longitudinal striations less distinct, the fibres small (particularly those from the foot and calf), and those from the foot notable "on account of the large amount of fatty connective tissue and on account of the considerable increase in the nuclei of the connective tissue."

For a full account of the clinical features of the case reference should be made to Spiller's article. The patient, a white male child, in its second year of age, was first seen by Dr. Spiller in May, 1904, was admitted to the University Hospital on July 15, 1904, and died August 5, 1904. Nothing of suspected import to the case was elicited in the family history; it was a full-term baby; nothing abnormal in the labor. Nothing untoward was noted in the development of the child after birth; but when about five months old, because of an apparent apathy and inattentiveness to objects usually attractive to such children, the eyes were carefully examined, and it was realized that almost complete blindness existed. The most notable feature of the case when first studied by Spiller (stated by the mother after close inquiry to have been present practically from birth) was a marked lack of muscular tone. With this existed absence of reflex movements. The child was never able to stand, to raise itself to a sitting posture, to hold any object in the hand, or to maintain a sitting position, save when carefully balanced, and then only for a few moments. The inferior members, which showed this flaccidity to a greater degree than the upper, could be without discomfort to the child bent forward on the trunk and the foot curved about the neck; and the leg could be bent anteriorly at the knee, so as to form an angle with the thigh. Voluntary movement was present but weak, and the muscles responded to faradaic stimulation. Death took place in a febrile accession of unknown nature, starting several days before death and reaching its maximum of 104° on the date of death.

The autopsy was performed the following morning by Dr. A. F. Coca, who noted the following gross features, referring the brain, cord, several peripheral nerves, and muscle, as above indicated, to Dr. Spiller for special study:

Body of male white infant of fair development for age, as above stated; slight putrefactive discoloration evident over lower part of abdomen; rigor mortis absent, and limbs flaccid, as described in life; no postmortem lividity; no œdema. Head large in proportion to body; eyes deeply sunken; pupils unequal (left, 2.5 mm.; right, 3.5 mm.). On preliminary incision moderate fatty panniculus; muscle substance pale, comparatively dry, notably flabby and rather poorly developed. Peritoneum smooth; no adhesions; omentum small, containing but little fat. Spleen weighed 12 to 15 gm., dark red in color; capsule free from adhesions, smooth and of normal thickness; organ of normal con-

[1] Monatsschrift f. Psychiatrie u. Neurologie, September, 1900.

[2] Ibid.

sistence; Malpighian bodies easily seen in cut section. Nothing abnormal noted in the gastrointestinal canal beyond the presence of a Meckel diverticulum, 4 cm. in length, situated 70 cm. above the ileocæcal valve. The mesenteric lymph nodes were much enlarged, pale, some slightly reddened,

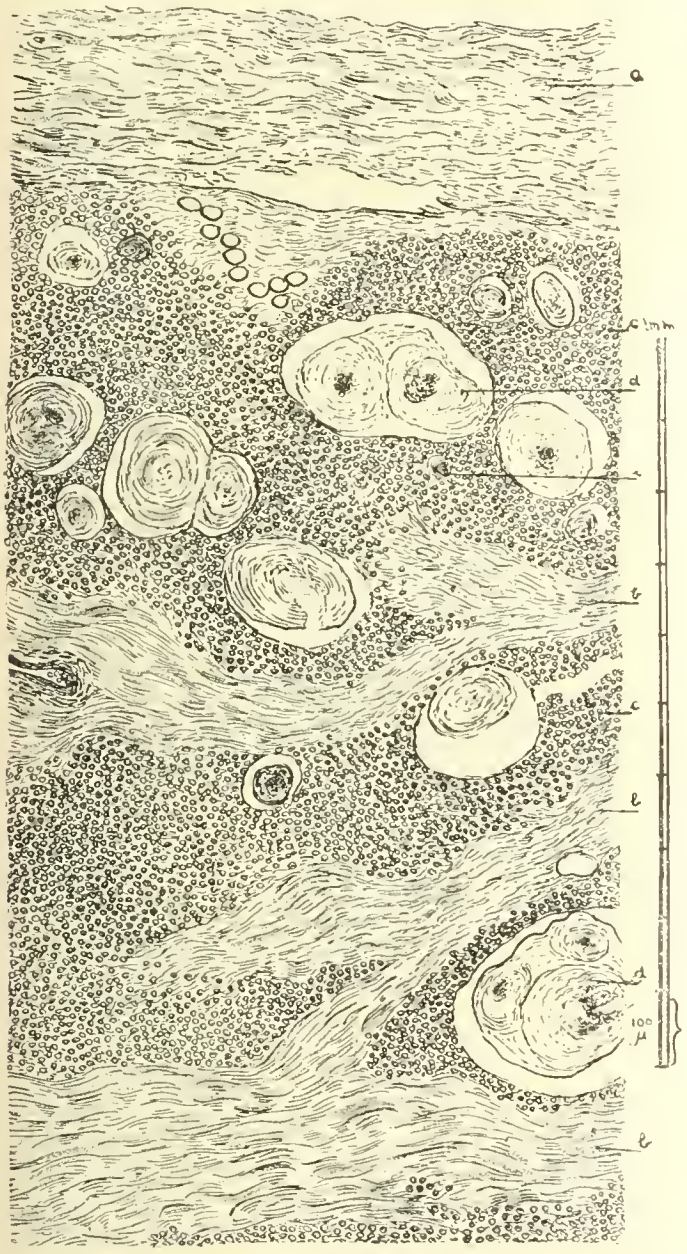

FIG. 1.—Low-power camera-lucida drawing of peripheral part of the thymus, showing the thickened capsule (*a*), the overgrowth of the fibrous trabecula (*b*), and the Hassall corpuscles (*c*), the largest reaching as much as one-fifth or one-fourth of a millimetre in diameter.

fairly firm, and not cheesy. The liver weighed 240 gm.; was of normal consistence, mottled yellow and red in color, with smooth and transparent capsule, and without noted gross lesions in the cut substance; the gall-bladder normal, containing a small amount of light, greenish-yellow bile. The pancreas grossly normal, soft, and of light-pink color. No gross changes recognized in the kidneys, ureters, or bladder. In the thorax note is made of the normal appearance of the pleural membranes; absence of gross lesions of the lungs, aside from slight hypostatic congestion of the dependent parts. The heart weighed 22 gm.; the wall of the left ventricle measured 7 mm.; myocardium pale, but firm; pericardium and endocardium normal throughout. Note was made of the absence of gross change in the thymus body.

For microscopic study, in addition to the parts referred to Dr. Spiller, bits of tissue from the following parts were retained, and in course of time prepared and examined: (*a*) thymus gland; (*b*) heart, wall of left ventricle; (*c*) lung, from unindicated non-congested portion; (*d*) liver; (*e*) pancreas; (*f*) spleen; (*g*) mesenteric lymph node; (*h*) kidney; (*i*) wall of bladder. Of these parts the heart wall, pancreas,

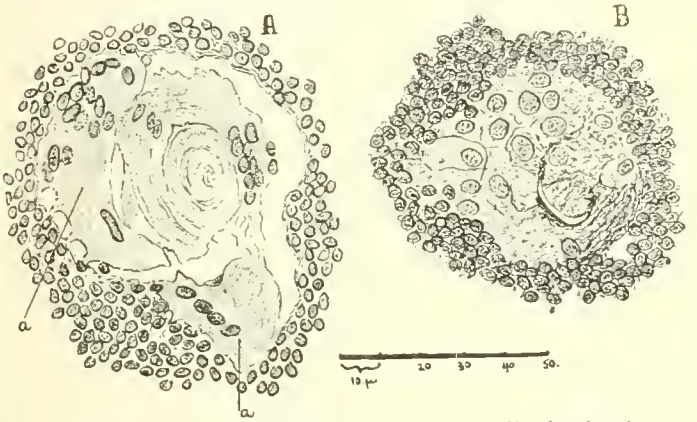

FIG. 2.—*A*. A moderate sized corpuscle of Hassall, showing its peripheral development; (*a*) giant cells at border of corpuscle. *B*. An islet of endothelioid cells, presumably from proliferation of endothelium of a lymph space and possibly one source of the Hassall bodies. A space in its central part is to be thought of as the nearly obliterated lumen of the space or sinus and the cells immediately about it are indefinite, have lost their nuclei, while those nearer the periphery of the islet are apparently younger, are more clearly nucleated, and probably are those in which further proliferation may take place.

kidney, and wall of the bladder show no recognized histological changes, and the liver is practically normal, beyond a slight fatty infiltration and a small degree of small round-cell infiltration about a few of the bile-ducts (embryonic connective-tissue cells).

The thymus body shows marked interlobular sclerotic changes, the sclerotic tissue appearing as loosely arranged hyaline bundles, each of these sending large hyaline fibrous trabeculæ into the interior of the lobules, dividing the latter until it is difficult to determine the outlines of the original lobules. Within the lobules the reticular structures are much increased as well, and the arteries almost invariably show some degree of fibrous thickening of the adventitia, a few also showing well-marked intimal fibrosis, with proliferation of the lining endothelial cells (others showing proliferation of endothelioid cells about the vessel-wall, probably of the cells

lining the perivascular lymph spaces). The usual arrangement of the lobules into a denser peripheral and looser central area is not maintained, the peripheral zone largely because of the prominence of the fibrosis, being, if anything, less lymphoid than the interior portion of the lobule. The lymphoid cells in themselves present no alterations, but a few mitotic nuclei were detected in them in different parts of the section. The most interesting feature of the section is the very large size and number of Hassall's corpuscles. These bodies with favorable light are in the larger instances recognizable by the unaided eye, some easily reaching 0.2 to 0.25 mm. in diameter. They occur indifferently toward the periphery or in the central portions of the lobules and often occupy a large proportion of its space. As a rule, they lie enclosed within thin but definite fibrous capsules, probably condensed reticular tissue of the surrounding lymphoid structures, each, as a rule, lying within a space probably the result of artefact, but generally attached at least on one side to the capsule. For the most part the larger examples are made up of several subordinate centres, around each of which the flat cells are concentrically packed; these subordinate ones fused together, with the peripheral cells enveloping the whole group. Often the centre of such a corpuscle selects a marked hæmatoxylin tint in a manner to suggest at least beginning calcification, the remainder of the corpuscle taking the eosin tint. Stained with carmine and subsequently submitted to the iron reaction with potassium ferrocyanide and hydrochloric acid, a few of the corpuscles show a small amount of blue granular matter, usually in the centre, but in some instances scattered in the outer portion, and occasional granules of the Prussian blue are to be found out in the lymphoid tissues of the general structure of the section. For the most part the concentrically packed cells show no trace of nuclear structure; but in many instances there are to be found on the outer portion of the corpuscle, or lining the capsule of the space in which the corpuscle lies, one or two layers of flat cells showing well-preserved nuclei, and occasionally in the centre of the body are a few cells preserving some nuclear appearances. In a few of the small bodies about the interior mass, usually poorly staining and hyaloid in appearance, are to be seen protoplasmic masses taking a light hæmatoxylin tinge and containing half a dozen or more nuclei, resembling ordinary giant cells or syncytia. There is no uniformity in the density of these Hassall corpuscles, some being quite dense, hyaloid, and showing but faintly the concentric lines of separation of the cells composing them, while others are extremely loose, with their scale-like cells more or less widely separated.

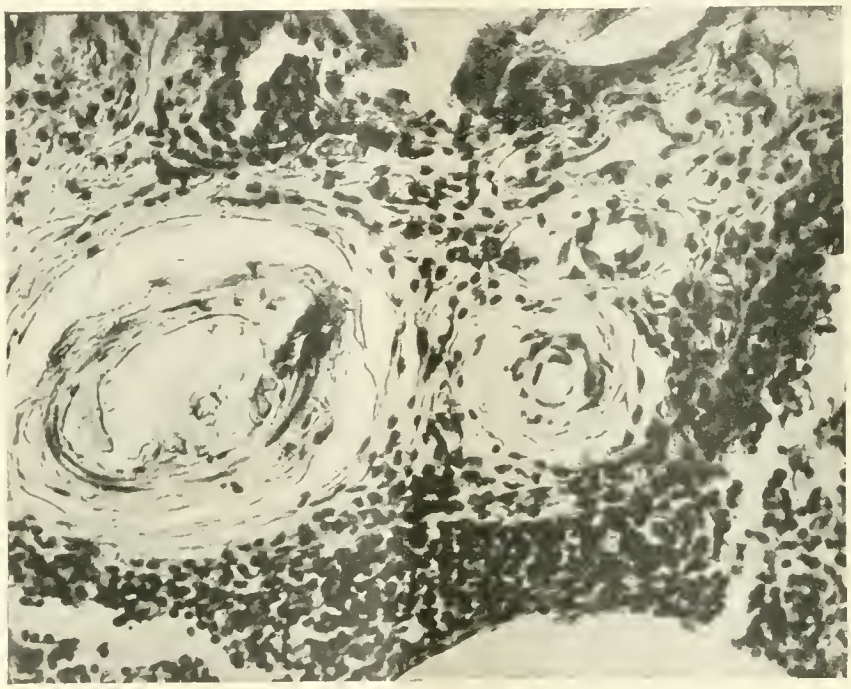

Fig. 3.—A moderate-sized Hassall corpuscle, showing the relatively younger and better preserved cells at the periphery.

Here and there in the midst of the lymphoid cells and without definite separation from them are islets of endothelioid cells, each such islet showing in its section from two or three to perhaps a dozen of these cells, suggesting the "germ centres" seen in ordinary lymph follicles.

In the section of lung submitted for examination no abnormality of the pleura or of the general pulmonary tissue is to be recognized, but along the heavier fibrous septa of the structure are occasionally found collections of lymphoid cells, one of which in the section is perhaps a millimetre in diameter and easily seen with the unaided eye; the rest microscopic.

These collections follow the type of ordinary lymph nodules, the larger one mentioned showing endothelial-lined channels resembling sinuses and small islets of endothelioid cells, reminding one of the germ centres of follicles.

In the spleen nothing of import is noted in the capsule or in the general splenic pulp, aside from moderate congestion of the latter. The trabeculæ are not thickened. Many of the vessel walls are unduly dense, sometimes actually hyaline, and some show distinct perivascular thickening from fibrosis. The Malpighian bodies are large; often in long section envelop the follicular arterioles for an unusual length; and a number show well-marked central endothelioid proliferation.

The mesenteric lymph nodes show on section a distinct excess of the lymph cells of the follicles and cords, the sinuses being practically occluded by these extracellular presences. No germinal centres are visible. The vessels are highly injected.

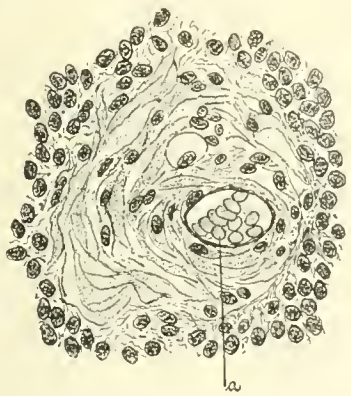

Fig. 4.—A bloodvessel containing red corpuscles (*a*) with marked proliferation of endothelium, the section simulating the appearance of a Hassall corpuscle in section.

The above findings, fibrosis of the thymus, with enlargement of the corpuscles of Hassall, endothelial proliferation in the thymus and in the Malpighian bodies of the spleen, arteriosclerosis noted in the thymus and in the spleen, the presence of lymph nodes in the lung and the proliferation of the lymphoid elements of the mesenteric lymph nodes, constitute undoubtedly interesting features of the case in hand. That they are an essential part or in any sense basic to the condition manifested in life by the muscular hypotonia can, of course, not be predicted from their discovery in this isolated case; but they unquestionably suggest the need for inspection in future investigations along the same line. *A priori*, from the theoretical view indicated by Oppenheim and confirmed by Spiller's positive findings in the present case, the muscular changes may be regarded at least tentatively as a definite feature of the affection. Our knowledge of the functions of the thymus and of its Hassall corpuscles, usually looked upon as vestigial rather than as essential elements with active function, is too vague to permit anything beyond a mere surmise, but it is not inappropriate here to keep in mind the general idea that the thymus, either by internal secretion or by destruction of untoward products of metabolism, has an influence upon the development of all or of parts of the body, either directly or through some action upon the trophic nervous power. One must further consider the possibility that back of all the changes described, muscular, as well as the alterations of the thymus, there may exist some condition of autointoxication, and it is conceivable that there might arise in the economy through faulty metabolism some material having stimulative influence upon the vascular and lymphatic endothelium, the proper lymphoid cells, and upon the connective tissues of vascular walls and of the thymus itself, and at the same time capable of so interfering with the trophic nervous influence as to give origin

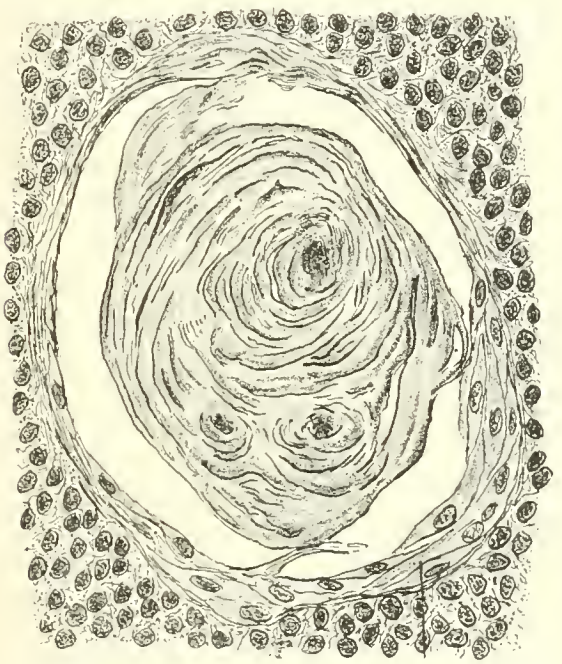

Fig. 5.—Photomicrograph of three small bloodvessels, the largest and intermediate ones containing blood cells, all showing endothelial proliferation (apparently of the perivascular lymph spaces) and simulating Hassall's corpuscles. (Zeiss, 16 mm. apochrom. obj.; No. 8, compens. ocular; camera length 80 mm.)

to the muscular faults indicated above. There is, of course, no proof of such a suggestion, but the features narrated from the case in hand are not incompatible with the idea. It should be added here that, while at the time of the autopsy the enlarged mesenteric lymph nodes were tentatively ascribed to tuberculosis, there was nothing in the gross features of the case, in the histological findings or in special preparations made with view of finding the bacilli, which in the least confirmed the supposition; and, on the other hand, while it is quite possible to encounter changes of the type here indicated in the mesenteric nodes and in the spleen secondary to comparatively simple intestinal changes, there was nothing found in gross inspection of the intestines or in the histological study of a small portion of the small intestine, fortunately retained by

Dr. Spiller and studied subsequently to the above investigations, which would lead to the conclusion that the intestine was the seat of changes primary to these splenic and lymphatic proliferations.

From an anatomical standpoint, the enlarged Hassall corpuscles are of especial interest. Their size and appearance, with the outer layer or two of their cells alone preserving nuclear structure, suggest that these bodies are not to be accepted as mere vestigial structures, but rather as actually growing bodies, developing by peripheral cell multiplication. The close similarity of some of the smaller bodies with some of the small bloodvessels with proliferated endothelium, the peculiar giant cells found at the borders of some of the corpuscles (much more commonly of connective tissue or endothelial origin than epithelial), and the occasional discovery of iron in the interior of these bodies, would add some weight to the view long since suggested by Afanassieff,[1] that these bodies are derived from proliferation of vascular endothelium.

[1] Archiv f. mik. Anat., 1877, Bd. xiv.

Not infrequently in the sections studied appearances are encountered suggesting the development of the bodies from such endothelioid islets as are noted as occurring in the midst of the lymphoid cells of the organ, and it seems quite possible that these areas should be regarded equally with the endovascular endothelium as capable of giving rise to the structures in question, these areas representing either "germ centres" or the proliferated endothelium of lymph spaces. Recent studies upon the development of the thymus and its corpuscles in guinea-pigs in the Biological Laboratory of the University of Pennsylvania and communicated personally to the writer by Dr. E. C. Conklin, conclusively indicate that these bodies are not epithelial vestigia; that, on the other hand, they do not normally develop from the vascular endothelium, appearing at a period when bloodvessels are not to be distinguished in the thymus, but that they take their origin from certain large, often branched, connective-tissue elements found in the organ, which are easily differentiable from the rest of its tissue by their staining reactions with Mallory's connective-tissue stain.

THE NATURAL DEFENCES OF THE ORGANISM AGAINST INFECTION.

By D. H. Bergey, M.D.,
Assistant Professor of Bacteriology, University of Pennsylvania.

The theory advanced twenty years ago by Metchnikoff to explain the defences of the organism against infection has been largely discarded in some scientific circles for those newer theories which are based upon detailed study of the mechanism of acquired immunity. The facts upon which Metchnikoff and his followers based their theory of the body defences have remained undisputed up to this time, but they are frequently disregarded in our discussions of the subject to-day.

It happens not infrequently that in our enthusiasm over the discovery of new and important scientific facts we lose sight of the ground that had been gained previously, and expend all our energies in the elaboration and elucidation of the newer and, therefore, frequently the more popular theories. Such a condition of affairs is seen to-day in our conception of the natural defences of the organism against infection. We have become so greatly infatuated with the normal bactericidal properties of the blood and body juices that we forget what had been learned with regard to the defences of the body before the bactericidal action of the blood serum had been discovered. The important work that had been done by Metchnikoff previous to the time of the discoveries of Nuttall, Buchner, and others is frequently ignored entirely in considering the body defences, or it is regarded in the light of an exploded theory.

It is not my object to detract from the work of Buchner, and of Ehrlich, and their followers, the results of which have been so helpful in elucidating the problem of immunity in general. I shall attempt rather to present the evidence at hand to show the limitations of the theory of the normal bactericidal action of the blood in accounting for the body defences, and present facts which seem to me to show that there is much more in the phagocytic theory of Metchnikoff than is to-day generally conceded to it by many of the workers in this field of labor.

Metchnikoff (*L'Immunité*, Paris, 1901, p. 84) divides the mesoblastic phagocytes of vertebrates into the fixed and free phagocytes or macrophages of the spleen, endothelium, connective tissue, neuroglia, and muscular fibres; and the free phagocytes, the leukocytes and lymphocytes, or microphages. It is impossible to know exactly the origin of the large phagocytes, and they are, therefore, designated simply by the name of macrophages. The two classes of phagocytes, the macrophages and microphages, are distinguished not only by their morphological characters, but also by their very marked physiological differences. All the phagocytes

possess amœboid movements, which give them the power of movement from place to place, or they possess the power of extending protoplasmic prolongations. The movements of different cells in the same group vary greatly according to their sensibilities. By means of a tactile sense the phagocytes possess a form of activity—chemotaxis—which permits us to distinguish the chemical composition of substances with which they are brought in contact. The existence of this chemotactic power shows that we must attribute to the amœboid cells an important role in the life of the organism.

The manifestation of variations in the chemotactic power of different classes of phagocytes has been demonstrated by the study of the nature of the cells that are attracted by different irritants. Great importance has been attached to the differences which result from inoculations of different bacteria. Salimbeni (*Annales de l'Institut Pasteur*, 1898, T. xii. p. 192) studied the leukocytosis in treated animals following the injection of different bacteria. After the injection of bacterium diphtheriæ the leukocytosis consists almost entirely of polynuclear cells, with only a few mononuclears. After the injection of cholera organisms the leukocytes are also of the polynuclear type, but after the injection of streptococcus pyogenes he found that a mononuclear leukocytosis is induced. Bresredka (*Annales de l'Institut Pasteur*, 1898, T. xii. p. 305) states that in diphtheria infection in children the polynuclear leukocytosis is so characteristic that it is possible to prognosticate the course of the disease by this means. Dembinski (*Annales de l'Institut Pasteur*, 1899, T. xiii. p. 426) found that in a pigeon inoculated with the avian tubercle bacillus the phagocytosis shows three stages: at first it is polynuclear, later mixed, and finally mononuclear in character. After inoculation with the human tubercle bacillus there is a mixed leukocytosis from the start which is followed by the formation of giant cells.

Experimentation has shown that normal blood serum possesses bactericidal, agglutinative, and antitoxic properties to a greater or lesser degree for a great variety of pathogenic bacteria. Usually these properties exist in normal blood serum in very limited quantities—quantities so small as to be often infinitesimal as compared with the condition of the blood serum in cases of acquired immunity. Now and then animals and persons are encountered that possess these properties to a much greater degree than usual, though they have not acquired immunity through recovery of a recognized attack of the disease in question. This fact was first pointed out by Bolton with regard to the content in diphtheria antitoxin of the blood serum of horses selected for the manufacture of the antitoxin. Many similar conditions have been reported, but it seems most probable that such an abnormal condition should be attributed to the acquirement of the immunity through recovery from an unrecognized infection. The limited bactericidal, agglutinative, and antitoxic powers of the blood serum occurring normally may be regarded in the light of an inherited property—a property which is transmitted in limited amounts from parent to offspring from generation to generation.

One of the strongest facts against the theory of Buchner, that natural immunity against bacterial infection is due entirely to the presence of specific bactericidal substances in the blood serum, is the demonstration that in the case of certain animals refractory to infection by certain organisms no such bactericidal power exists in their blood. This was very forcibly brought out by Zabolotnoff (*Annales de l'Institut Pasteur*, 1904, T. xviii. p. 527). He has demonstrated that the immunity of the guinea-pig against the bacillus of swine erysipelas is not due to the presence of a specific immune body in the blood serum of the animal, but that the protection is due entirely to phagocytosis; the polynuclear leukocytes, followed apparently by the mononuclear leukocytes, achieving the digestion of the bacteria. Again, the marked tolerance of the rat to diphtheria toxin, and that of the chicken to tetanus toxin, is not due to the presence of antitoxin in the blood of these animals, but merely to a marked affinity of certain cells of the body for these toxins, thus protecting the cells of the central nervous system against the action of these poisons.

Bail (*Centralblatt f. Bacteriologie*, Bd. xxxvi., xxxvii.; *Arch. f. Hygiene*, Bd. lii.) has recently published exhaustive studies on infection with bacterium anthracis, bacillus typhosus, and with the cholera organism. His studies have been carried out on normal as well as on treated animals. As the result of his studies he has formulated his so-called *aggressin* theory, according to which the disease-producing properties of an organism are dependent upon the degree to which it has acquired aggressive powers to overcome the natural defences of the body. His studies have convinced him that the natural defences of the body are in large part cellular in their nature, and that the aggressive power of an organism against the cellular elements permits it to induce pathogenic effects.

Kikuchi (*Arch. f. Hygiene*, Bd. lii.) studied the augmentation of the aggressive powers of bacterium dysenteriæ by means of intraperitoneal inoculation of guinea-pigs. The injection of non-fatal doses resulted in the production of a hyperleukocytosis, consisting at first of small mononuclear cells, and later of large numbers of small polynuclear cells, and finally of macrophages. After death from fatal doses Kikuchi collected the peritoneal exudate, rendered it free from bacteria by centrifugating and treating with toluol. The exudate, treated in this manner, when injected along with a non-fatal dose of bacteria, induced the death of the animal; and this effect is attributed to the "aggressin,"

supplied by the exudate, assisting in the pathogenic effect of the non-fatal dose of bacteria injected.

Kikuchi states that it is possible for the aggressin to act in three ways: 1. Disturbance of the leukocytes, in that it may have somewhat the property of the leukocidin found by Van de Velde in the staphylococci. 2. Inhibition of the phagocytosis. 3. Exclusion of the leukocytes, or a negative chemotactic action like that found by Bordet and Massart (*Annales de l'Institut Pasteur*, 1891, T. xv.) in the metabolic products of bacteria. The latter possibility is the only one which Kikuchi believes comes into action. He believes that the aggressin does not affect the life nor the activity of the leukocytes, but merely prevents them from reaching the field of action.

The interesting studies which Wright and Douglas (*Proceedings of the Royal Society of London*, 1903, vol. lxxii. p. 357; 1904, vol. lxxiii. p. 128) have reported demonstrate that the leukocytes of themselves are incapable of taking up bacteria. They have shown that the blood serum contains something which is necessary in order to permit the function of phagocytosis to manifest itself. This substance, which is normally present in the blood, they have named opsonin (opsona, I cater for; I prepare victuals for), and has the property of acting on bacteria in such a manner that the leukocytes can gain access to them and take them up into their bodies. If the serum is heated to 50–55° C. it loses this property. The leukocytes are then no longer able to manifest their phagocytic properties. These discoveries of Wright and Douglas have been substantiated by Hektoen and Ruediger (*Journal of Infectious Diseases*, vol. ii. p. 128), and they have also brought forth evidence which indicates that "opsonin, like toxins and complements, possesses two groups of molecules: one haptophore, whereby it attaches itself to the bacterial receptors, and one which may be called the opsoniferous group, whereby is effected in the bacterium some change, physical or chemical, that is necessary for phagocytosis." The observations of Wright and Douglas have also been confirmed by Bulloch and Atkin (*Proceedings of the Royal Society of London*, 1905, vol. lxxiv. p. 379).

In the course of an investigation upon the pathogenic properties of bacterium pseudodiphtheriticum for guinea-pigs, I have been forcibly impressed with the influence of the phagocytic cells of the body in preventing infection. My results have shown that this organism is very well adapted for the study of this phase of the body defences against infection. With organisms of low degree of virulence the cellular reactions are far more characteristic than with more highly virulent organisms, because with the highly virulent organisms the cellular reaction appears to be overpowered in a short time and the animal succumbs to the inoculation.

My studies were made by means of intraperitoneal injections of large quantities of the non-virulent organisms. Following such an injection there is induced a marked extravasation of leukocytes, principally of the polynuclear type, and these englobe the bacteria very rapidly, so that frequently after forty-eight hours none of the bacteria remain extracellular; at least, so far as can be demonstrated by microscopic examination of the exudate. Not all the bacteria are killed by this time, since it is still possible to obtain growth in cultures, though usually only a few colonies develop from a drop of the exudate. Many of the bacteria within the phagocytes do not take on stain, and hence they are probably dead, though numerous phagocytes are encountered which are packed with bacteria that stain very readily.

The peritoneal exudate of these animals also contains a relatively small number of small mononuclear leukocytes and usually a much greater number of erythrocytes.

In addition to the foregoing another most interesting group of cells is encountered. These are large mononuclear cells which manifest marked phagocytic powers in that they are frequently seen packed with the other cellular elements of the exudate. These are the so-called macrophages of Metchnikoff, and apparently have the special property of clearing up the field of battle between the bacteria and the microphages. Many specimens of these large phagocytes may be seen in a drop of the exudate which contain two or three polynuclear phagocytes filled with the bacteria, as well as one or more erythrocytes. In many of these large phagocytes the ingested cells are seen to be undergoing digestion in that they show disintegration of their protoplasm and fragmentation of the nuclei.

My studies have convinced me that, in at least some forms of infection, the most important protective properties are exerted by the cellular elements of the body in preventing infection. In other infections it is possible that the normal antitoxic, agglutinative, and bactericidal properties of the blood play the more important role, but in the light of the experimental evidence at hand it seems probable that these are not the only factors in overcoming infection, as some investigators are inclined to assume.

My studies upon bacterium pseudodiphtheriticum have shown that by repeated inoculation into guinea-pigs it is possible to so augment the aggressive powers of these organisms that the animals succumb in less than twenty-four hours. In the peritoneal exudate of an animal inoculated with a virulent culture the picture is quite different from that seen in the peritoneal exudate after inoculating a non-virulent organism. After death from the inoculation of the virulent organisms the peritoneal exudate is poor in cellular elements, and these cells frequently show little evidence of phagocytic power, practically all the bacteria being extracellular. The results obtained with the virulent organisms appear to give strong support to the aggressin theory of Bail, since the differences in the results obtained with injections of

virulent and non-virulent organisms suggest the probability that the differences noted are due to the acquirement of aggressive powers by the bacteria.

The fact that relatively few phagocytes are present in the peritoneal exudate after inoculation with virulent organisms appears to bear out the contention of Kikuchi that the aggressive properties acquired by the bacteria are of the nature of negative chemotactic properties. It appears that the leukocytes are in some way prevented from reaching the point where the bacteria are acting, and hence multiplication of bacteria and consequent infection take place. It appears, however, that there is also an inhibition of phagocytosis, because the leukocytes that are present in the peritoneal exudate on postmortem examination usually show little evidence of phagocytic activities. It seems probable that the acquirement of virulence on the part of an organism rests upon these two factors: inhibition of phagocytosis and negative chemotaxis; and in the light of the studies of Wright and Douglas there seems to be some evidence that the inhibition of phagocytosis is of a nature of an antiopsoniferous action. This action, however, cannot be due to the presence of an antiopsonin in the true sense, but is most probably due to direct chemical effect on the opsonin.

In the light of these facts it is probable that the body cells possess a far greater protective power in warding off disesae than do the blood serum and the body fluids. It is only when the bacteria have acquired a high degree of resistance to phagocytosis, or when overwhelming doses of less virulent organisms are introduced, that the phagocytic powers of the leukocytes are overcome.

INTRAHEPATIC GALL-BLADDER.*

By Henry S. Wieder, M.D.,
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(From the Anatomical Department of the University of Pennsylvania.)

At the present time, when the surgery of the gall-bladder is occupying so much of the attention of surgeons in general, it may not be amiss to call attention to an anomaly of that organ which, when encountered during an operation, is liable to complicate matters to a very great if not insuperable degree; that is, "intrahepatic" gall-bladder. The specimen which called the attention of the writer to the condition and which he wishes to report was obtained from a case of his friend, Dr. Lowenburg, to whom he is indebted for the privilege of reporting it.

The patient was a child, aged fifteen days, the cause of whose death was not determinable, clinically, with a certainty, the child being apparently healthy until the day of death, when it suddenly became cyanosed and died shortly afterward. Autopsy showed nothing abnormal, excepting a patulous foramen ovale and this anomalous condition of the liver and gall-bladder, which has no clinical significance in this case.

The liver was found in its normal position, apparently not enlarged, measuring 10 x 6.5 x 3.5 cm., not adherent to any of the surrounding viscera, and almost completely enveloped by peritoneum, except for a very limited extent upon the posterior surface. The convex surface is smooth, of a dark-brown color, and shows the Liebermeister grooves produced by the ribs. The relative size of the right and the left lobes is about normal.

Situated 5 mm. above the free edge of the right lobe of the liver, and 3 mm. to the left of the fissure which replaces the usual notch for the gall-bladder, is seen a small, almost circular, slightly elevated green cyst, which, upon being opened, allowed the escape of bile (Fig. 1). Examination of the lower surface of the liver shows the gall-bladder deeply embedded

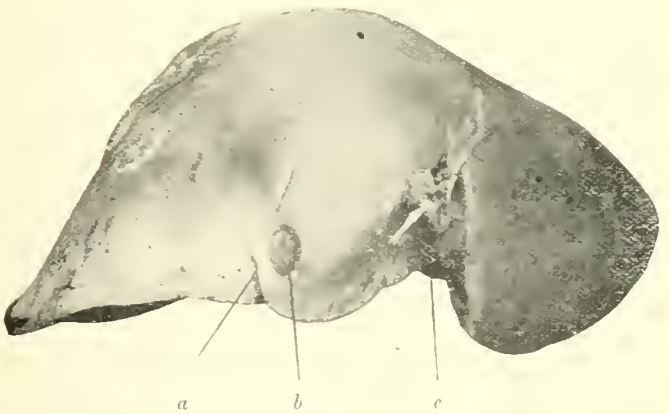

Fig. 1.—*a*. Fissure for gall-bladder. *b*. Gall-bladder. *c*. Fissure for round ligament.

in the floor of the fissure bearing its name, but not covered by hepatic tissue. Five mm. from its termination the fissure deviates to the right and the gall-bladder leaves it, plunging into the hepatic tissue to appear on the convex surface, as previously described. In this manner the fundus of the gall-bladder becomes entirely surrounded by liver tissue, a bridge

* Read before the Philadelphia Pathological Society, May 25, 1905.

of hepatic tissue 5 mm. in thickness separating it from the free margin of the liver.

In addition to the above rare anomalous condition, there are also four anomalous fissures to be seen upon the under surface of this liver. One is a shallow fissure, 2.7 cm. in length, taking its origin from the fissure for the round ligament and running parallel to and 2 cm. from the free margin of the left lobe of the liver (No 1, Fig. 2). Another very small and shallow fissure, 8 mm. long and branching at its centre to form a Y, is found on the left side of the fissure for the round ligament near its anterior termination (No. 2, Fig. 2). The third fissure, 12 mm. long and 5 mm. deep, taking its origin from the transverse fissure, is found in the right lobe running forward and to the right (No. 3, Fig. 2). The fourth and last fissure is found connecting the fissure for the gall-bladder with the fissure for the round ligament, thus bisecting the quadrate lobe. It is 2 to 5 mm. deep and runs 12 mm. from and almost parallel to the free margin of the quadrate lobe (No. 4, Fig. 2).

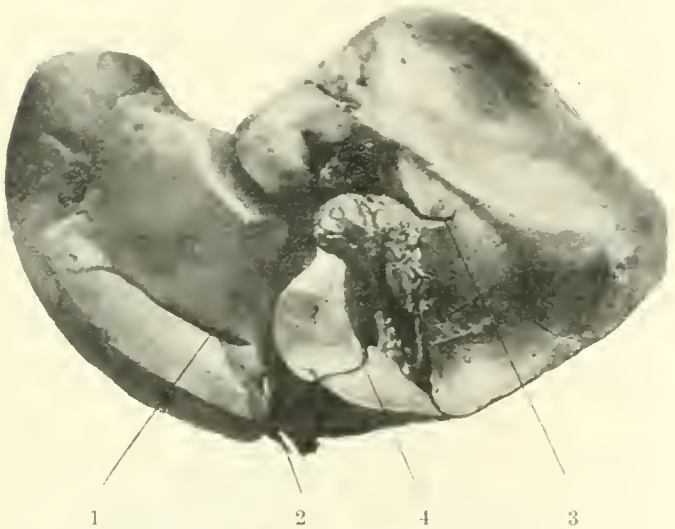

Fig. 2.—Anomalous fissures upon under surface of the liver.

Before concluding the description of the liver, the attention of the reader is called to the great depth of the fissure for the round ligament (Fig. 1), being 2 cm., while the bridge of hepatic tissue connecting the right and left lobes is only about 1.5 cm. in thickness. The umbilical vein is still patulous.

The writer has taken the liberty of calling the situation of this gall-bladder "intrahepatic," the name given it by Dévé,[1] in order that there may be some uniformity in the reports of this peculiar and interesting condition. A rather careful review of the lietrature as far as the resources of the library of of the College of Physicians would permit, fails to reveal any reference whatever to the condition here seen until 1903, when it was reported by Dévé before the Anatomical Society of Paris.

In a study of 130 infants, with the object of ascertaining the relative frequency of this condition, he encountered it in a dozen cases, and he marvels at the fact that it has never been recorded before. His paper reviews the matter very thoroughly, and we may, with considerable profit, review its most important points. He has divided the cases in which it occurs into the following three classes:

1. Those in which the tip of the fundus of the gall-bladder dips into the hepatic substance, but does not make itself evident upon the convex surface of the liver (No. 3, Fig. 3).

2. Those in which the fundus of the gall-bladder buries itself in the hepatic tissue, but does not appear on the convex surface as a distinct cyst, but as an elevation covered by a very thin layer of liver tissue which is slightly bile-stained and thereby differentiated from the surrounding hepatic tissue (No. 4, Fig. 3).

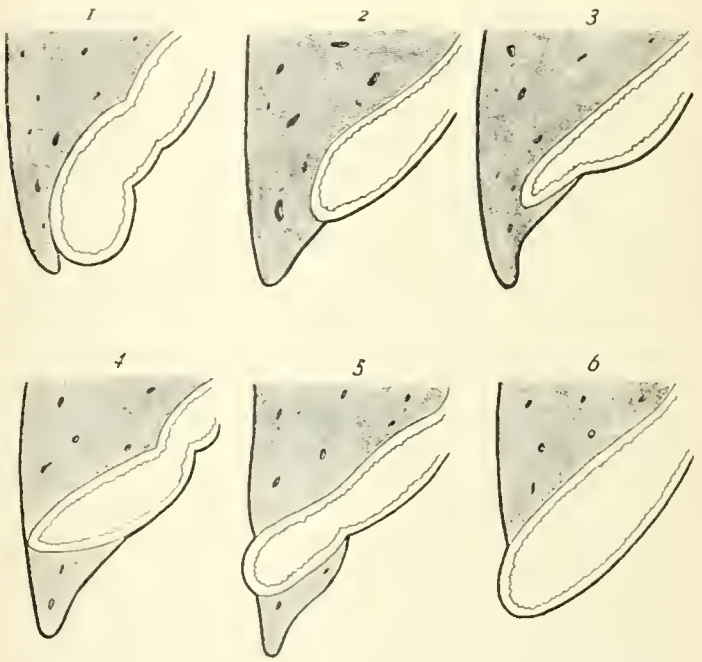

Fig. 3—1. Normal disposition of the gall-bladder as seen on cross-section. 2, 3, 4, and 5. Various types of intrahepatic gall-bladder. 6. Resultant condition seen in adult life.

3. Those in which the fundus of the gall-bladder pierces the liver tissue and appears on the convex surface as a cyst, as is shown in Fig. 1 and No. 5, Fig. 3. Fig. 3 illustrates Dévé's idea and is taken from his article.

In the majority of these cases the fundus of the gall-bladder alone is the portion of the organ involved, so that there may be some objection to the name intrahepatic gall-bladder. Dévé defends the title on the ground that the extent of gall-bladder enveloped varies, he having seen at least one case in which the gall-bladder was buried in the liver tissue for two-thirds of its extent. He makes the positive statement that this condition is found only in infants, and explains this by atrophy of the bridge of hepatic tissue, owing to the mechanical action of the distending gall-bladder pressing up against

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the anterior abdominal wall. He substantiates this statement with observations upon adult livers in which he found the gall-bladder in a deep groove and at the level of the fundus he found vestiges of hepatic tissue with vessels disappearing in the neighboring parenchyma.

The above statement the writer believes is true in the great majority of cases, having seen a specimen in the Pathological Laboratory of the University of Pennsylvania, showing the gall-bladder deeply grooving the fissure for the gall-bladder,* with obliteration of the usual hepatovesicular *cul-de-sac* at the fundus of the organ. The pathological records of the University of Pennsylvania also contain the record of one of Dr. Riesman's cases, autopsy performed by Dr. Smith, in which the gall-bladder was found in a very deep notch on the anterior aspect of the liver, the notch being so deep that the lowermost portions of the gall-bladder were not below the edge of the liver. As further evidence that this was probably in infancy an intrahepatic gall-bladder, the liver tissue directly above the gall-bladder was very thin and parchment-like and more of grayish hue than the remainder of the liver.

While, as the writer has stated before, and has endeavored to prove by the cases cited, he believes that this condition does not occur very frequently in the adult, nevertheless, the statement of Dévé that it never occurs except in infancy is wrong, as is shown by the cases recently reported by O'Day[2] and Lemon.[5] O'Day's case, similar anatomically to the one shown in Fig. 1, occurred in an adult and was found on the operating table during an operation for gallstones.

Lemon's case was much more remarkable. It was encountered during an operation for gallstones by Dr. W. K. Bouton, of Melbourne. To quote Lemon's description, "after opening the abdomen (the liver presenting itself in the operation wound), what appeared to be a hydatid cyst was seen on the anterior surface of the right lobe—a slightly rounded elevation of pale-yellowish color. On lifting the liver forward a similar though somewhat more projecting eminence appeared on the posterior (inferior) surface which, when viewed through the substance of the liver, was quite translucent. It was in the normal position for a gall-bladder, but the surfaces, both anterior and posterior, were continuous with liver substance. As no gall-bladder could be discovered, an incision was made on the posterior (inferior) surface into the swelling, when bile gushed out, and on further exploration two large gallstones, one barrel-shaped and the other conical, were secured; there was an additional facet on the barrel-shaped stone, showing that a third stone had been present, but as a probe passed the whole length of the common duct without striking one, it had evidently been passed previously. The edge of the incision into the gall-bladder at the time of operation was at least three-eighths of an inch thick, the circularly arranged coat of the gall-bladder being marked off very definitely from the liver substance on the one hand and from the mucosa, etc., of the bladder on the other." This is, without doubt, the most marked, and, in fact, the only true case of intrahepatic gall-bladder ever reported, and still it was found in an adult.

In addition to refuting the statement of Dévé, those two cases, since they both contained gallstones, demonstrate two very important facts, viz., that when the condition persists into adult life it is most liable to be the seat of gallstones, and that the contractile power of the normally free gall-bladder probably has much to do with the prevention of the formation of gallstones. It is the opinion of the writer that the gallstones were present in these cases and will probably be present in all cases of intrahepatic gall-bladder in adult life, because of the fact that the organ has rigid walls and is therefore unable to expell any excess of mucus, inspissated bile, etc., that may be present as a result of hyperæmia or some slight catarrhal condition of the mucous membrane. This mucus or inspissated bile forms a favorable site for the growth of bacteria that may gain access to the gall-bladder or favorable nidus for the further deposit of cholesterin and bile salts, and thus we have the formation of stones. Again, having no contractile power, the gall-bladder is unable to expell stones when formed; so that they probably give no symptoms until the organ becomes overfull or one, by gravity, becomes engaged in the cystic or common duct. Occurring in adults, as we have seen, this condition becomes important from the etiological standpoint in its relation to gallstones and from the operative standpoint. It is very easy to realize how such a condition or even the more superficial disposition of the organ described by Dévé as occurring in adults, may seriously hamper the surgeon in operating upon it.

Dévé makes the statement that in these cases of intrahepatic gall-bladder the fissure for that organ is never seen on the anterior aspect of the liver, but that its place is taken by an elevation of the free margin of the liver. This also the writer thinks may be true in the great majority of cases, but that it is not always the case is shown by the specimen shown in Fig. 1, for in it that fissure can be seen as a distinct incisure of the free margin about 5 mm. long.

The cases of Dévé, O'Day, and Lemon are the only recorded cases I have been able to find, but as the result of enquiry, I have found that Dr. Hand, of this city, encountered a case a few years ago in a child about seven years of age. This case has not been reported, but was similar in the relations of the gall-bladder to the one reported in this article.

The only fact that now remains to be considered is the cause of this peculiar disposition of the gall-bladder. A cursory examination is sufficient to convince one that it is not a pathological condition, but that it is rather some congenital misplacement, the cause of which is rather hard to explain.

When we consider that the gall-bladder is an outgrowth from the bile-duct beginning about the second month,[3] and that the bile-duct itself is an outgrowth from the duodenum separate from and independent of the liver, and if we accept the conclusion of Thompson, who says: "The gall-bladder appears to develop along the bottom of a fissure (in the liver), which extends forward to the anterior border and which apparently is formed prior to the appearance of the vesicle," the most plausible explanation that suggests itself is that offered by Dévé. He believes it is the result of the general tendency of the human liver toward the obliteration of the various interlobular fissures which are so marked in the majority of mammals. Thus we get a union of the quadrate lobe with the right lobe in the same manner as the two primitive lobules of the left lobe are united to form one, and in the process of this union, which takes place after the full growth of the gall-bladder, the fundus of that organ is surrounded by liver tissue. Until a better explanation is forthcoming, the one of Dévé will probably have to stand, in spite of the fact that in this case there has been no obliteration of the fissure for the gall-bladder and there is a tendency for the fissures not to close, as evidenced by the four anomalous fissures and the great depth of the fissure for the round ligament.

References.

1. De quelques particularities anatomiques et anomalies de la vesicule biliaire, par le Dr. F. Dévé, Bulletins et Mémoires de la Société Anatomique de Paris, 1903, S. 6, tome v. pp. 261 and 266.

2. Gall-bladder Through Foramen in Liver, by J. C. O'Day, Oil City, Pa., The Journal of the American Medical Association, April 22, 1905, No. 16, vol. xliv. p. 1281.

3. Diseases of the Liver and Gall-bladder, by H. J. Waring.

4. Fissures of the Gall-bladder, by J. Thompson, Journ. Anat. and Phys., vol. xxxiii. pp. 47 and 64

5. Anatomic Peculiarities of a Gall-bladder and an Appendix, F. Lemon, Hawthorne, Australia, Lancet, London, May 13, 1905.

AN INVESTIGATION UPON THE NATURE OF THE BACTERIA IN THE FILTERED WATER SUPPLY IN PHILADELPHIA.

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Not very many years ago those who were interested in caring for the public health looked upon the presence of bacillus coli in water with a great deal of concern. Though they did not regard the organism itself as particularly pathogenic to man, it was thought to be an important indication of sewage-polluted water, and it was at this time that the presence of the organism in any amount was considered sufficient to condemn a water and that processes for their isolation were first given to the scientific world.

The methods in use to-day still include the incubation at 37.5° C. of a small volume of the water in a litre or more of sterile bouillon to which a weak solution of phenol has been added, as suggested by Vincent[1] in 1890, or by inoculation of a solid medium containing litmus and sugar, with known quantities of the suspected water, plating it, and isolating the typhoid-colon group of colonies from these plates, as recommended by Wurtz,[2] at about the same time.

It was in 1890, too, that Theobald Smith[3] first introduced the fermentation tube into bacteriology, since which time it has played a very important role in the detection of the typhoid and the colon bacilli, and the separation of the members of the latter group from one another, by observations of the gas formulæ. It has also been of great use in estimating the number of organisms of the bacillus coli group contained in a given quantity of water. Smith was induced to invent a method of examining a water quantitatively for the presence of bacillus coli therein contained by observing that the practice of incubating large quantities of water and adding phenol broth was not a fair test for the purity of a water, claiming that colon bacilli could be found in any water if the sample taken were sufficiently large. The fermentation tube method, which was the result of his labors along this line, has made it easy for us to determine the number of bacteria of the colon group in 1 c.c. or less of the water under examination.

Distribution of Bacillus Coli. We know from the experiments of numerous investigators that bacillus coli is not found in the human intestine alone. Percy Frankland,[4] in speaking of the occurrence of bacillus coli in water, says: "This organism is, in fact, frequently found in great numbers in polluted streams as well as in well waters into which the drainage from dungheaps has penetrated, while in pure waters it is but rarely met with."

Dyar and Keith[5] found it in the intestines of dogs, cats cows, and hogs; Fremlin,[6] in the feces of dogs, rabbits, and mice, but not in guinea-pigs, rats, and pigeons. It has also been found, after death, in the organs of fowls. E. B. Hoag,[7] working in the laboratory of Professor Russell, found

the organisms in the feces of a great number of animals and in some birds.

Many bacteriologists, among whom was Kruse,[8] have held that bacillus coli was not characteristic of the intestine at all, but was a saprophyte having a wide distribution of nature. Beckmann[9] isolated, in 1894, bacillus coli from the city water of Strassburg, which derives its supply from a ground water allowing no possibility of fecal contamination. Refik,[10] in 1896, found it in cisterns, wells, springs, and waters of all kinds around Constantinople. He concluded from these investigations that fecal contamination can only occasionally account for the presence of bacillus coli in water, saying that these organisms in ground waters are due to their general distribution all over the earth, being deposited by the dust of the air, or in the upper layers of the earth, which may be one of its normal habitats, and are filtered through into the ground waters. Great caution should be exercised, he says, in condemning a water on account of the presence of bacillus coli, unless they are there in great quantities.

Weissenfeld,[11] a pupil of Kruse, after examining 30 samples of supposedly pure water and 26 samples of water known to be contaminated, concluded that bacillus coli could be found in any water if the sample taken were large enough. His methods for detecting the colon bacillus were entirely unreliable, however, and the results of his work contradict his own conclusions, for in 24 out of the 26 samples of contaminated water he isolated what he determined by his own imperfect methods to be bacillus coli; while in only 8 out of the 30 samples of good water could he find the organism.

R. Burri[12] states that the use of so great a quantity as one litre for the detection of bacillus coli would condemn many a good water. Other observers, among whom was Theobald Smith, held that the *number* of colon bacilli present in a water should always be taken into account before condemning it. On this point Smith[13] says that the mere presence of bacillus coli does not prove that the pollution is of human origin, nor, indeed, that the water is not suitable for drinking purposes, but the number of colon bacilli in a given quantity of water is the all-important thing to know before condemning it.

The presence of bacillus coli in soil and ground waters is easily explained by the fact that the earth may be contaminated by the feces of birds flying over it and of human beings and animals traversing it constantly, and, as a result, the filtering through the substrata of the colon bacilli into the ground waters.

Pakes[14] concluded, after an exhaustive study of the question, that deep well water should contain no colon bacilli whatever, but that other water, unless containing the organism in 20 c.c. or less, should not be condemned.

Again, Horrocks[15] asserts that water polluted with sewage in so great a dilution as 1:100,000 will contain bacillus coli, and that unless the organism can be isolated from 20 c.c. or less the water had probably been polluted with sewage, but the pollution was not recent.

Prescott,[16] in examining 47 different cultures of lactic acid bacteria from washings of cereals, etc., found 53 per cent. of them to give the typical reaction for bacillus coli, and concluded that "too much reliance must not be placed on the so-called colon test for potable waters." Prescott, however, as well as other observers who drew conclusions as he did, did not take into consideration, in applying the colon test, the number of bacilli in a given quantity of water.

Perhaps, as has been suggested by many investigators, bacillus coli may have originally been a saprophyte widely distributed in nature, but even if this be so, and the intestine is only a secondary habitat, it is certain that the organism finds this habitat more agreeable than any other for its development, inasmuch as a vast majority of the colon bacilli in nature are found there. Hence it seems safe to say that colon bacilli found in water supplies find access to them through contamination of the water or soil by animal pollution.

Winslow and Hunnewell,[18] after having examined 157 samples of water from supposedly unpolluted sources, found typical colon bacilli in only 5 instances, and paracolon also 5 times, in the 157 1-c.c. samples. From this they conclude that bacillus coli is very rarely found in 1-c.c. samples of unpolluted waters, and that a parallelism exists between the number of colon bacilli present in a water and the extent of its contamination.

Occurrence of Bacillus Coli in Filtered Waters. For several years past the colon test has been largely used for the determination of the efficiency of sand filtration, and of natural purification through the flow of streams.

In 1899 Fuller[17] found bacillus coli in 60 per cent. of the 1-c.c. samples obtained from the Ohio River at Cincinnati, while after slow sand filtration through the city filters the same water was found to contain bacillus coli, in 50-c.c. samples, in about one-half the whole number of examinations.

The report of the Massachusetts State Board of Health for 1898 shows that the Merrimac River at Lawrence contained, as an average for the year, 47 colon bacilli per 1 c.c. before filtering, while out of 117 samples taken after passing through the city filter the organisms were found in only 9 instances, and then in but a single colony.

In 1899 the average number per 1 c.c. at the intake, in 180 samples, was 47, and 103 at the Lawrence experiment station, a short distance below. This was reduced, after filtering and settling, to 7 per cent. of the original number, and after distributing through the pipes to the experiment station, to 4 per cent. of the original.

In 1900 the results were about the same.

In repairing the filter beds at Lawrence, in 1900, the sand on some of them was seriously disturbed, and shortly after the completion of this work, in December, bacillus coli was found in 72 per cent. of the samples after the water had passed through the filter. In January and February the percentage was reduced to 54 and 62 respectively, while in March in only 8 per cent. of all samples taken was bacillus coli found. This is about the normal for that water.

Parallel with this excess of colon bacilli in the water supply, during January, there were 59 cases of typhoid fever, in February 12, and in March only 9, all during the first part of the month.

For 1903 the number of colon bacilli found in the effluent of the Lawrence City filter was as follows: Bacillus coli occurred only 10 times in the 238 1-c.c. samples taken during the year, and only 31 times in the same number of 100-c.c. samples. This would show bacillus coli as appearing in only 4.2 per cent. of the 1-c.c. samples and 13 per cent. in the 100-c.c. samples. The Lawrence City plant, which consists of slow sand filters, therefore is seen to possess a very high degree of efficiency, as judged fron this standpoint.

Let us now compare the efficiency of this slow sand filtration with that of a so-called mechanical filter, constructed at Lawrence early in 1903, through which water from the Merrimac River was passed at an average rate of from 24,000,000 to 47,000,000 gallons per acre daily, using sulphate of alumina as a coagulant. With the amount of coagulant varying from time to time from one-half grain to two grains per gallon, they observed that the average number of colon bacilli, from May 26th to October 16th, inclusive, in the raw river water was 108 per 1 c.c., while in the water from the effluent of the filter the average percentage of samples containing bacillus coli during the investigation was 17.3 in the 1-c.c. samples and 27.6 in the 100-c.c. samples.

The efficiency of the mechanical filter was at times very great, but it was shown to be subject to great and sudden variations which could not be accounted for, while the slow sand filtration showed a steady, low, colon count. Another disparaging feature about the mechanical filter was that it was necessary to add so great an amount of the coagulant as to make the effluent acid in order that the water might be rendered free from color.

In examining spring water from 99 springs in 1900 the Massachusetts State Board of Health reports that after examination of 4 samples from each spring, 2 taken directly from the spring and 2 from the bottles as supplied to the public, in the water from 1 spring bacillus coli was found twice—once from the spring direct and once in the bottled sample. This spring was in the woods, but unprotected from surface drainage, and the manner of bottling subjected it to contamination. In 5 other samples bacillus coli was found in that taken by the inspectors from the spring direct. All of these springs were liable to pollution from houses or manured fields, and 4 out of the 5 were shown to be unfit for use as drinking water by chemical analysis. In 7 other spring waters bacillus coli was found only in the samples from the bottles; 3 of these were exceptionally pure, but contamination was easy in the process of bottling.

Jordan[19] has made an exhaustive study of the bacillus coli test in the self-purification of streams. His results coincide pretty closely with those of Brown[20] and Fuller[17] and indicate that in large rivers, where sewage is in great dilution, bacillus coli may be isolated in about one-half the number of 1-c.c. samples examined. Such river waters are, of course, not safe for drinking purposes unless filtered or boiled beforehand.

Bacillus coli, as we have seen, is without doubt a sewage organism, and therefore, when found in water, is a sure index of sewage pollution. Klein and Houston[21] have emphasized this fact, and by this means they have shown that the presence of sewage in water can be demonstrated to a much finer degree than by chemical examination. The detection of pathogenic organisms is impossible by chemical examination, and the amount of pollution possible of detection by bacteriological methods is 10 to 100 times less than that detectable by chemical methods.

Water containing no colon bacilli in 100 c.c. may be said to be very pure, but the presence of bacillus coli in so small an amount as 1 c.c. should be sufficient to condemn a water.

Streptococci in Water. A. C. Houston,[22] after examining 46 different soils—virgin and polluted—for the presence of organisms characteristic of sewage, concluded that virgin soils do *not* contain spores of bacillus enteritidis sporogenes, bacillus coli, nor streptococci, or, at most, in very small numbers, but that soils polluted with human or animal excrement *do* contain all three of these typical sewage organisms in abundance. He considers the presence of streptococci in water as evidence of recent and dangerous animal pollution. They are absent, he says, in even large quantities of pure water and virgin soils. They lose their vitality quickly and die when physical conditions are unfavorable and comprise species highly pathogenic to mankind. They are present in human feces and crude sewage in great numbers, and are very abundant in soil and water recently contaminated by human beings and animals.

However, all streptococci are not delicate, nor are all pathogenic. Houston found streptococci in 0.001 c.c. of crude sewage, in one milligram of human feces, and in very small quantities of soil and water recently polluted with animal dejecta. The findings and conclusions of Houston point to the fact that the test for streptococcens in water is the most delicate that has yet been found, and is almost certain proof of recent animal, and therefore dangerous, pollution.

The relative abundance of streptococcus in water must

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also be carefully considered. If it be absent in 10 c.c. of a water of a fair degree of purity and present in 0.001 c.c. of crude sewage, the distinctions to be drawn between water and sewage allow us a fair margin on which to establish a standard, so as not to impair the value of the test. As a rule, however, the presence of streptococcus indicates *very* recent animal pollution, while the presence of bacillus coli represents less recent, though not at all remote, animal pollution.

Further, inasmuch as bacillus typhosus is a hardier germ than the streptococcus, the presence of streptococcus indicates that the conditions between the time of pollution and the time of collection of the sample were not unfavorable for the development of the organism of typhoid fever. This cannot be said of bacillus coli, however, for it has been shown to possess greater vitality than bacillus typhosus.

Houston's own conclusions as to the significance of bacillus coli and the streptococcus in water are as follows:

"As a matter of fact, through observation, the relative abundance of bacillus coli in pure and impure substances is so amazingly different as to lead us to suspect that not only does bacillus coli not flourish in nature under ordinary conditions, but that it tends to lose its vitality and die. In brief, I am strongly of the opinion that the presence of bacillus coli in any number, whether in soil or water, implies recent pollution of animal sort. But is there a microbe (or class of microbes) which, by its presence, implies animal pollution of extremely recent and therefore dangerous pollution? The streptococcus, in my judgment, is to be thought of in this sense."

The streptococcus of sewage was first reported in this country by Winslow and Hunnewell.[23] It was isolated by them in a study of bacteria found on the hands of school children, and since then in fresh human feces and in Boston sewage. D. M. Belcher, a student in the laboratory of the Massachusetts Institute of Technology, also found it in a study of the bacteria in a septic tank.

Winslow and Hunnewell's work agrees with that of Houston in that the great importance of the presence of streptococcus in water as an index of recent animal pollution is established.

Knowing that the water supply of the laboratory is filtered through the new sand filters constructed a year or more ago by the Department of Public Works of the City of Philadelphia, it was suggested to the writer that a detailed study, over a period of time, of the water, both as to the quality and quantity of the organisms found, would be instructive as to the efficiency of the system of filtration in this city as well as interesting as a study in itself.

Although the number of organisms present has a very important bearing on the potability of a water, still it is almost universally held that the nature of organisms present is of much greater significance in determining its suitability for drinking purposes.

Methods Employed. The bacteriological examination of the water was begun on January 7, 1905. Samples were obtained from a spigot in the laboratory, from which the water had been allowed to run for twenty minutes before a specimen was taken in a sterile test-tube. Plates of agar-agar and of nutrient gelatin were made, and, for a while, of lactose-litmus agar. Three tubes of agar and of gelatin were inoculated and plated; into the first tube was placed, by means of a sterile pipette, 0.5 c.c. of the water; into the second, 1.0 c.c.; and into the third, 1.5 c.c. The plates of agar were incubated at 37.5° C. for twenty-four hours, when the colonies which had developed in the mean time were counted; while the colonies on the gelatin plates were allowed forty-eight hours in which to develop, at a temperature of about 18° C.

The lactose-litmus agar, to which 1 c.c. of the water had been added, was tried for several days, but finding this method of detecting the colonies of bacillus coli unsatisfactory its use was discontinued.

At the time of making the plates 1 c.c. of the water under examination was placed into a fermentation tube containing 2 per cent. glucose bouillon. If any gas appeared in the closed arm of the tube within forty-eight hours, at a temperature of 37.5°, plates of agar were made from these tubes, incubated for twenty-four hours, and, at the end of that time, examined for the presence of bacillus coli. Sub-cultures were made of all doubtful colonies found upon the plates of agar and of gelatin made directly from the water, and upon the agar plates made from the fermentation tubes.

Some short method had to be decided upon for the differentiation of bacillus coli from others which had very much the same appearance in sub-cultures made from the plates, and the following is the one resorted to. If the cultures had the following characteristics they were set down as bacillus coli:

1. Gas production in glucose bouillon.
2. Acidification and coagulation of milk.
3. Production of indol.
4. Growth on agar, bluish-white, transparent.
5. Gelatin, not liquefied.
6. Reaction in the serum media of Hiss, viz., rendering acid and coagulating lactose, glucose, maltose, and mannite, and leaving saccharose and inulin unchanged.

The sewage streptococcus of Houston was carefully sought for in smears made from the sediment in the fermentation tubes inoculated after January 22d, and if found, as it was in a number of instances, as seen in the accompanying table, an attempt at isolation was made. This, however, was clearly successful in only two cases—they being isolated on agar, in bouillon, milk, and gelatin from fermentation tubes in which gas had been evolved of the dates of February 17, 1905, and March 22, 1905, after having been incubated

at 37.5° C. for forty-eight hours. Several attempts were made to have the organism grow on potato, but they were all unattended with success.

In many instances where the streptococcus was found in the smear from the fermentation tube, upon isolation only diplococci were found, and no chains of even three or four elements could be discerned, as a consequence of which the term streptococcus could not be applied to them.

It will be interesting to note that the number of colonies was, as a rule, greater on gelatin plates than on those of agar, showing that some of the water bacteria grow more readily at the temperature of the room than at incubator temperature. It will also be seen that though the count averaged considerably less than 50 organisms per 1 c.c., the American standard of purity for filtered water, there were found typical colon bacilli in more than 50 per cent. of the samples taken. On plates which showed the presence of bacillus coli not only one colony of the organism, but many, as a rule, were found.

The presence of the sewage streptococcus was also demonstrated in many instances, though isolation could be made in only two of the samples. These findings seem to indicate that the filtered water is still polluted by accumulations in the mains. Such accumulations of filth should be thoroughly flushed out to avoid contaminating the filtered water. Under existing conditions the best way of preventing the entrance of pathogenic bacteria into the body through drinking water is to boil the water before drinking it.

Conclusions. We have seen from the reports of the Massachusetts State Board of Health that, in the filtered water of the city of Lawrence, bacillus coli has been found during the past several years, in from 4 to 7 per cent. of all the samples examined. These results show a very high state of efficiency for a filter working with a water such as that of the Merrimac River, which abounds with so much sewage and factory pollution.

The water of the Ohio, after having passed through the new sand filters of Cincinnati, when examined by Fuller in 1899, showed bacillus coli in 50 per cent. of the 100-c.c. samples.

In all of our work only 1-c.c. samples were used, and in about 50 per cent. of these colon bacilli were isolated. This shows that the filters were operating on a rather low grade of efficiency.

In no other work has the writer been able to find a report on the presence of streptococci in filtered water, but, from the fact that 24.13 per cent. of the 1-c.c. samples examined showed the presence of these organisms, it appears to serve as an important additional test of the presence of sewage pollution.

The results of the first month are not at all satisfactory, but it is probable that this must be accounted for largely from the fact that the water pipes of the laboratory contained many bacteria which were finally removed by the daily flushing. If we take the results in the fermentation tube for the second and third month we find they are far more satisfactory. During the second and third month 21 out of 50 samples showed fermentation, or 42 per cent; while bacillus coli was isolated from some of the samples which did not produce fermentation.

Table Showing Detailed Results of Analyses.

Date. 1905.	Colonies per c.c. on plates of agar.	Colonies per c.c. on plates of gelatin.	Gas produced with 1 c.c. water.	Kinds of organisms on plates.	Kinds of organisms in fermentation tube.	Streptococcus of sewage.
Jan. 7	131	—	+	1, 2, 3, 4, 7, 8	2, 7	
" 9	118	409	+	1, 2, 4, 7	7	
" 10	80	162	—	1, 2, 3, 4, 5, 6, 4		
" 11	92	25	+	1, 2, 3, 4, 5, 14	1	
" 12	31	15	+	1, 2, 3, 4, 5, 12, 13	1, 2, 5, 7	
" 13	19	97	+	1, 2, 3, 4, 12	1	
" 14	36	74	+	1, 2, 5, 7, 15	1, 4, 5	
" 16	27	56	+	1, 2, 4, 13, 15	1, 2, 4	
" 17	36	41	+	2, 4, 5, 14	1, 7	
" 18	21	20	+	1, 2, 4, 5	1, 2, 4, 7	
" 19	19	—	+	2, 4, 5	2, 7	
" 20	10	49	+	1, 2, 4	2, 16	
" 21	17	23	+	1, 2, 4, 5, 12	1, 2, 7	
" 23	10	9	—	1, 2, 3, 5	.....	—
" 24	19	13	+	1, 2, 7	1, 2, 5, 7	—
" 25	12	12	+	1, 4, 5	1, 4, 5, 7	—
" 26	8	85	+	1, 2, 5	1, 2, 5	—
" 27	8	55	+	1, 2, 4, 5, 7	1, 2, 4, 5, 7	—
" 28	8	10	+	1, 4, 8, 12	1, 4	—
" 30	6	48	—	1, 2, 5	.....	+
" 31	5	20	—	1, 2, 4	.....	—
Feb. 1	9	8	+	1, 2, 4, 5, 12, 15	7	—
" 2	6	42	—	1, 4, 5	.....	—
" 3	10	40	+	1, 2, 5, 7	1, 2, 7, 12	—
" 4	13	9	—	1, 2, 4, 5, 7	.....	—
" 6	6	14	—	1, 2, 3	.....	—
" 7	8	6	+	1, 2, 5	2	—
" 8	8	5	+	1, 2, 7	1, 2	—
" 9	6	9	—	1, 2, 3, 4	.....	—
" 10	6	18	—	1, 9	.....	—
" 11	8	10	+	1, 2, 3, 7	1, 7	—
" 13	7	Lost	—	1, 7	.....	—
" 14	5	"	+	1, 4	1, 4, 5, 7, 10	+
" 15	6	"	—	1, 2	1, 5	—
" 16	9	"	—	1, 2, 5, 11	.....	—
" 17	7	22 (4 days old)	—	1, 2, 5	1, 2, 5, 7, 10	+
" 18	8	102 (5 days old)	—	1, 2, 4, 7	.....	—
" 20	8	33 (3 days)	—	1, 2, 5, 7	10	+
" 21	11	14	+	1, 2, 3, 4, 5	1, 7	—
" 23	10	10	—	1, 2, 5	.....	—
" 24	8	15	—	1, 2, 5	.....	—
" 25	14	7	+	1, 2, 3, 4, 5, 7	1, 2, 3, 4, 5, 7	
" 27	9	23	—	1, 2, 3, 4, 5, 12	.....	—
" 28	8	28	—	1, 3, 5	1, 4, 5	—
Mar. 1	8	28	+	1, 3, 5	1, 7	+
" 2	12	35	—	1, 2, 3, 4, 5	.....	—
" 3	11	41	—	1, 2, 3, 5	.....	—
" 4	16	35	—	1, 2, 5, 7, 12	1, 2, 5, 9	·
" 6	11	47	—	1, 2, 5	.....	—
" 7	13	13	—	1, 2, 5	.....	—
" 8	10	15	+	1, 2, 5	1, 2, 5, 7	—
" 9	9	17	—	1, 2, 5	.....	—
" 10	15	61	+	1, 2, 5, 7, 13	1, 2, 5, 7, 17	—
" 11	26	83	+	1, 5, 7	1, 5, 7	
" 13	28	+	+	1, 5	1, 7	—
" 14	43	93	+	1, 2, 3, 5, 7	1, 7	—
" 15	10	87	—	1, 5	.....	—
" 16	12	24	+	1, 3, 5	1, 5, 7	·
" 17	12	—	—	1, 2, 4, 5	.....	—
" 18	13	38	+	1, 2, 3, 7	1, 7	—
" 20	18	15	—	1, 2, 3, 4, 5, 13	1, 2, 3, 4, 5, 7	Diplococci.
" 21	18	49	—	1, 2, 3, 5, 7	.....	
" 22	19	45	+	1, 2, 3, 5, 9, 10	1, 2, 5, 9, 10, 7 1, 5, 7, 12, 15	Diplococci.
" 23	16	50	+	1, 5, 7	Strep.	+
" 24	29	—	+	1, 2, 3, 5, 7	1, 2, 3, 5, 7, 12	+
" 25	31	—	...	1, 2, 5	1, 2, 5,	Diplococci.
" 27	17	18	—	1, 2, 3, 4, 5, 7	1, 5, 9 or 10	Diplococci.
" 28	19	44	—	1, 2, 3, 5, 7	1	—
" 29	11	41	—	1, 2, 5	1, 5	—
" 30	12	46	—	1, 2, 5, 7	.....	—
" 31	18	161		1, 2, 4, 5, 7	7	Diplococci.
April 1	27	42	+	1, 2, 3, 5, 7	1, 5, 7	—

I wish to express my gratitude to Dr. D. H. Bergey, Assistant Professor of Bacteriology in the University of Pennsylvania, for his many valuable suggestions and his constant interest in this work.

List of Bacteria Isolated from the Water. (1) Bacillus cereus; (2) Bacillus mesentericus; (3) Bacillus mycoides; (4) Bacillus megatherium; (5) Bacillus subtilis; (6) Bacillus proteus vulgaris; (7) Bacillus coli; (8) Cladothrix; (9) Staphylococcus albus; (10) Streptococcus; (11) Bacillus pinatus; (12) Bacillus aurescens; (13) Mic. fervidosus; (14) Bacillus formosus; (15) Bacillus alkaligines; (16) Bacillus lactis aërogenes; (17) Bacillus subflavus.

Bibliography.

1. Vincent, A. Sur un nouveau procédé d'isolement du bacilli typhique dans l'eau. Compt.-rend. Soc. de biol., 1890.

2. Wurtz. Note sur deux charactères differentiels entre le bacilli d'Eberth et le B. coli commune. Arch. de méd. exp., 1892, vol. iv. p. 85.

3. Smith, T. Das Gährungskölbchen in der Bakteriologie. Centralblatt f. Bakt., 1890, Bd. vii. p. 502.

4. Frankland, P. and C. G Micro-organisms in Water, 1894.

5. Dyar and Keith. Notes on Normal Intestinal Bacilli of the Horse and Certain Other Domesticated Animals. Technology Quarterly, 1893, vol. vi. p. 256.

6. Fremlin. Vergleichende Studien an Bakterium Coli Commune Verschiedener Provenienz. Arch. f. Hyg., 1893, vol. xix. p. 295.

7. Russell and Basset. Significance of Certain Gas-forming Bacteria of Non-colon Type in Sanitary Water Analysis. Pro. Am. Pub. Health Assoc., 1899, vol. xxv. p. 570.

8. Kruse, W. Kritische und Experimentelle Beiträge zur hygienischen Beurtheilung des Wassers. Zeitsch. f. Hyg., 1894, vol. xvii. p. 1.

9. Beckmann, W. Ueber die typhusähnlichen Bakterien des Strassburger Wasserleitungswassers. Arch. für Exp. Path. u. Pharmak., 1893–1894, vol. xxxiii. p. 466.

10. Refik. Sur les divers types de coli bacille des eaux. Ann. de l'Inst. Pasteur, 1896, vol. x. p. 242.

11. Weissenfeld, J. Der Befund des Bacterium Coli im Wasser und das Thier experiment sind Keine brauchbaren Hülfsmittel für die hygienische Beurtheilung des Wassers. Zeit. f. Hyg., vol. xxxv. p. 78.

12. Burri, R. Nachweise von Fäkelbakterien in Drinkwasser. Hyg. Rund., 1895, vol. v. p. 49.

13. Smith, T. Water-borne Diseases. Jour. N. E. Water Works Assoc., 1896, vol. x. p. 203.

14. Pakes, W. C. C. The Application of Bacteriology to Public Health. Public Health (London), 1900, vol. xii. p. 385.

15. Horrocks, W. H. Bacteriological Examination of Water. London, 1901.

16. Prescott, S. C. On the Apparent Identity of the Cultural Reactions of B. Coli Communis and Certain Lactic Bacteria. Science, 1902, vol xv. p. 363.

17. Fuller, G. W. Report on the Investigation into the Purification of Ohio River Water for the Improved Water Supply of the City of Cincinnati, 1899, p. 41.

18. Winslow and Hunnewell. A Study of the Distribution of the Colon Bacillus of Escherich and of the Sewage Streptococci of Houston in Polluted and Unpolluted Waters. Journ. Med. Research, 1902, p. 502.

19. Jordan, E. O. The Relative Abundance of B. Coli Communis in River Water as an Index of the Self-purification of Streams. Journ. of Hyg., vol. i. p. 295.

20. Brown, C. C. Report on Mohawk and Hudson Rivers. Thirtieth Ann. Rep. State Board of Health, N. Y., 1893, p. 680.

21. Klein and Houston. Report on Bacteriological Evidence of Presumably Recent and therefore Dangerous Sewage Pollution of Elsewise Potable Waters. Sup. XXVII. and XXVIII. Ann. Rep. L. G. B. Med. Off. Rep., 1897–1899.

22. Houston, A. C. Chemical and Bacteriological Examination of Soils, with Reference to the Amount and Nature of Organic Matter, and the Number and Character of Bacteria Contained in them. Sup. to XXVII. Ann. Rep. L. G. B., containing Rep of Med. Officer for 1897–1898, p. 251. Sup. to XXVIII. Ann. Rep. L. G. B., containing Rep. of Med. Officer for 1898–1899, p. 439; Sup to XXIX. Ann. Rep. L. G. B., containing Rep. of Med. Officer for 1899–1900, p. 593.

23. Winslow and Hunnewell. Streptococci Characteristic of Sewage and Sewage-polluted Waters. Science, 1902, vol. xv. p. 827.

FRACTURES OF THE HEAD OF THE RADIUS. AN EXPERIMENTAL STUDY AND REPORT OF CASES.*

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(Concluded from page 197.)

ANATOMY.

To appreciate the importance and difficulties associated with a study of fractures of the head of the radius a practical knowledge of the elbow-joint is necessary. The capsule of the elbow by blending with the orbicular ligament includes both the elbow proper and the superior radioulnar articulation. In the former only flexion and extension are permitted, in the latter only pronation and supination. The anterior and posterior portions of the capsule are weaker than the lateral, the posterior, the weaker of the two, being thin and membranous. To permit the normal range of motion, according to the degree of flexion or extension, one or the other must be relaxed; so that a small intracapsular fragment of bone, as from the articular surface of the humerus, may have a considerable range of movement within the joint. This is not so with the usual detached fragment of the head of the radius, the orbicular ligament never being relaxed. The lateral ligaments are much stronger than the anterior and posterior, and are never normally relaxed, so that there is no lateral movement in the elbow-joint. It should be borne in mind that while the internal lateral ligament is strongly attached to the ulna below, the external has no such attachment to the radius. Its fibres passing downward from the external condyle become almost lost in the orbicular ligament, only a few

* Read before the Philadelphia County Medical Society, June 14, 1905.

fibres being reflected to the neck and head of the radius. It is not quite as strong as the internal ligament.

The radial head articulates with the capitellum of the humerus, and follows the ulna in flexion and extension, while it rotates independently of the ulna. In full extension the head of the radius becomes more prominent posteriorly, and can be felt as a prominence in the dimple below the external condyle posteriorly. Only that part of the head which is anterior, therefore, is in contact with the capitellum in that position. In full flexion the anterior part of the head strikes in the depression of the humerus immediately above the capitellum.

The superior radioulnar articulation has but one special ligament, the orbicular. This with the lesser sigmoid cavity of the ulna forms a complete circle enclosing the head of the radius. No ligament in the body so closely and completely embraces a bone as does the orbicular ligament of the head of the radius, and at the same time permits so free a range of movement. It has considerable strength, being the only ligament holding the head of the radius to the ulna. It blends intimately with the external lateral anterior and posterior portions of the capsule, which further strengthen it. That this is a firm articulation is shown by the fact that in posterior dislocations of the elbow the radius is rarely separated from the ulna. The lower edge of the ligament is united to the neck and head of the radius by a thin membranous layer which is loose enough to permit free rotation of the head before becoming taut. The superior radioulnar articulation reaches as low as the upper end of the radial shaft, so that the head is intra-articular as low as the narrowest part of the neck. Only the cup-shaped upper surface and vertical border are covered with articular cartilage, to the lower edge of which are attached the reflected fibres of the capsule, and at that level the periosteum is lost in the articular cartilage. From the lower edge of the cartilage to the neck, the bone is covered by reflected capsule and periosteum, the capsule being lined with synovial membrane. The vertical articular border varies in depth in different portions of the circumference. When the forearm is in supination the internal portion which is in contact with the lesser sigmoid cavity of the ulna is deepest. From the lower edge of the cartilage to the neck the bone slopes gradually, except at the internal or deepest border, where the change is more abrupt and the attachment of the capsule strongest.

The importance of this arrangement of the capsule lies in the fact that when a portion of the radial head is broken off, it very likely still retains its attachment to the capsule. (See Fig. 3.) In every experimental fracture that I produced, not only was the fragment so attached, but the attachment was complete along the whole lower border; so that in a similar case in life, the blood supply would have been ample to maintain the nutrition of the fragment.

Bruns[4] says that, when the fracture is confined to the head, it is purely intracapsular and that the fragment lies loose in the joint, or is attached by a band of the capsule as in his and Huter's cases. He found three cases in the literature in which the fragment had been converted into a free articular body. Judging from my experimental work it is evident that at the time of the accident, at least in uncomplicated cases, the fragment is not loose, except for the line of fracture. In none of them was it movable enough, when the orbicular ligament was in place, to warrant calling it a loose fragment;

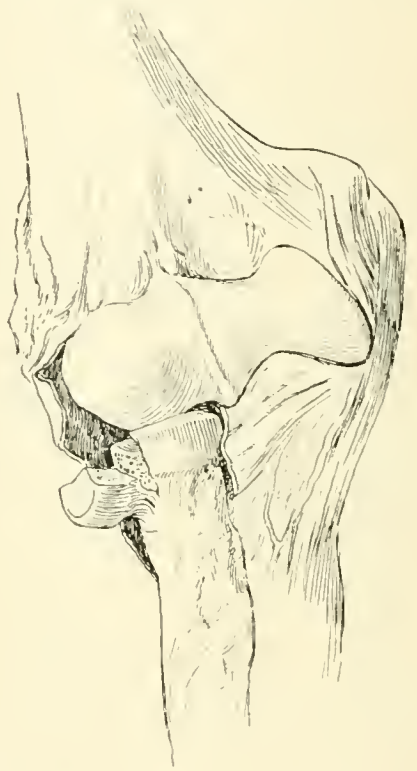

Fig. 3.—The substantial attachment of the small, loose fragment to the periosteum and reflected portion of the orbicular ligament is shown in this illustration. This attachment was present in every experimental fracture produced by the writer, and is noted several times among the cases reported in the literature. The wedge-shape of the small fragment is again evident.

and in most of them it was decidedly fixed and could not be moved in the slightest degree from its normal position.

Stimson[22] says: "I should make immobilization more complete and maintain it for a longer time than for simple fracture of the coronoid process, because the vitality of the fragment can be preserved or regained only by the spread into it of granulations coming from the main portion, and the more perfect the quiet the more probable would be the accomplishment of this desired result." One would infer from this that the fragment was entirely detached and deprived of its blood supply until it had formed adhesions with the rest of the head.

In the uncomplicated variety if the fragment is torn from

its capsular attachment, I believe that this will not occur at the time of the accident, but later from rotation of the head, as, for instance, in the attempts to make a diagnosis, particularly under an anæsthetic, the detached fragment becoming caught in an injured portion of the capsule, and refusing to follow its fellow. Such an accident will probably be very rare, if it occurs at all.

I have found only one case, not compound, in the literature (Stimson) in which suppuration of the joint resulted, and this was in a weak, strumous lad, and no case in which it was shown that necrosis of a fragment resulted.

FREQUENCY.

The statement of Bruns, that this fracture is probably much more frequent than is generally supposed, has been supported by the opinions of several writers, who have given the subject attention. Owing, chiefly, to the difficulties in diagnosis, no one has yet brought out definitely any information as to the frequency of this fracture.

We know that fractures of the lower end of the radius are among the most common that occur, and, as we pass upward, fractures of it become less common. As we approach the elbow they become more obscure, because the bone is there more deeply placed and more difficult to examine; except in the depression on the surface below the external condyle posteriorly, where the head is very superficial. The difficulties in diagnosticating fractures of the head are further increased by the fact that it is in close contact with the ulna and humerus, small fragments of which may be broken off. By far the most important factor confusing the diagnosis is the close approximation of the fragments by the orbicular ligament, which is probably intact in the majority of cases.

The difficulties in diagnosis account for the apparent infrequency. Although the skiagraphic evidence on this point is still very scanty, it has already demonstrated that this fracture is so frequent that it demands greater attention on the part of the profession than it has yet received.

Ross and Wilbert, as already stated, have published three series, each of 500 consecutive fractures of the extremities as shown by the skiagraph. An examination of these statistics gave very interesting information as to the frequency of this fracture. As the writers say, these statistics are apt to be influenced by the local conditions, as the class of industrial plants from which a large proportion of the accidents are derived. They will also be influenced by the fact that frequently doctors send to hospitals, for skiagraphic evidence, only those fractures which are difficult of diagnosis, so that the frequency of the obscure fractures are abnormally high. For instance, I observe that the number of fractures of the clavicle is only 11 in the first series, 13 in the second, and 11 in the third, or 35 in all, or about 2 per cent. Gurlt quoted by Stimson, collected statistics from the London Hospital, making them up from the annual reports from 1842 to 1877, in which the percentage of fractures of the clavicle was 15 per cent., or about 20 per cent. of the fractures of the extremities.

In the skiagraphic statistics it is worth noting that in the case of fractures of the clavicle, shaft of the humerus, and the patella, there is little variation in the numbers in the three series, which would tend to confirm the general accuracy of the statistics.

There were 9 fractures of the shaft of the humerus in the first series, 10 in the second, and 9 in the third, or 28 in all.

Of fractures of the patella, there were 5 in the first, 5 in the second, and 7 in the third series, or 17 in all.

In the first series there were 8 fractures of the head and neck of the radius, 7 in the second, and 3 in the third, or 18 in all.

For purposes of comparison we are confronted with the apparent difficulty that the first series includes fractures of the neck of the radius with the fractures of the head. Bruns[4] says that the fracture of the head is well differentiated from that observed occasionally in which there is a transverse fracture of the neck, the head being entirely separated from the diaphysis, and the injury being called a fracture of the neck of the radius.

If this were so, we still have the fact established that the fractures of the head are more frequent than is generally conceded. Comparison with the numbers of fractures of the shaft of the humerus, and of the patella in the last 1000 cases, shows 19 of the humerus, 12 of the patella, and 10 of the head of the radius.

While I was not successful in producing a fracture of the neck of the radius by the same force with which I did the fractures of the head, I believe that they are due to the same cause, most commonly, a fall on the hand. Von Bergmann[39] says of these fractures of the neck of the radius: "In regard to the etiology and mechanism, accurate observation and investigation are lacking."

Stimson, in his work on fractures, discusses them together, and says that he knows of only 1 case (Mutter) of fracture of the neck without splitting of the head. In Dr. H. K. Pancoast's collection of skiagraphs at the University of Pennsylvania, I selected two in which the upper end of the radial shaft was, in each case, impacted into the head. The head was much depressed, in each, below its normal level, particularly on the outer side. This depression shows, I think, that the head had been driven downward by the impact of the capitellum, as in a fall on the hand. I have a good picture of one of them taken more than a year after the accident (see Fig. 4), and by it one can see that the forearm is approximately in supination, and that the external

part of the head is markedly lower than the rest of the head. This depressed portion corresponds approximately to the position of the detached fragment in the usual fracture of the head. In pronation this depressed portion would be anterior, and would then correspond to the point of impact of the capitellum of the humerus in falls on the hand. We

Fig. 4.—Skiagraph of one of Dr. Pancoast's cases, taken about fifteen months after the accident. This was selected instead of the original one, taken about ten days after the accident, because of the obscurity in the latter produced by the callus which was then present. The typical deformity observed in fractures of the neck is well shown. Evidence of old fracture of the head, which is very frequently associated with fracture of the neck, is seen on the upper surface of the head. The external angulation of the elbow, observed in several of the cases reported in the literature, is slightly shown here. It is due to the depression of the head, which is caused by shortening of the radius at the seat of fracture.

can easily conceive of the whole head being tilted downward and forward, the neck giving way instead of the usual detached portion of the head, which is anterior at the time of the fall. There is firm union in this case in spite of the history of persistent movements of the part from the time of the accident, and for a time at least at the hands of a masseur, which indicates that impaction must have existed. This impaction in itself points strongly to a fall on the hand as the cause of the fracture. I observe that the antero-posterior diameter of the neck is slightly less than the lateral diameter, when the forearm is in the prone position. The neck is therefore less resistant to the force applied to it in falls on the hand in the prone than in the supine position.

In the Mutter Museum of this city are two specimens of fracture of the neck of the radius. In one of them, probably the specimen referred to by Stimson, there is marked angular deformity at the seat of fracture, which is just above the bicipital tuberosity. The head is considerably deformed, and, I believe, shows distinct evidence of previous fracture. The whole specimen consists of the bones of the upper extremity from the shoulder down. The forearm, I should say, is in extreme supination. The whole head is depressed as in Dr. Pancoast's two skiagraphs of fracture of the neck, and approximately the same part of the head is much more depressed than the rest, and about to the same extent. This depression is most marked about posteroexternally, whereas in the skiagraph it is apparently external. This difference is probably due to the fact that one cannot determine in a skiagraph absolutely the position of the forearm by the position of the bones, and the fact that the depression will vary according to the position of the forearm. In this specimen the most depressed portion would be anterior in pronation, and would correspond to the point of impact of the capitellum in a fall on the hand. I therefore argue that a fall on the hand was the most likely cause of the fracture of the neck in this specimen. In one of Dr. Pancoast's cases there is a distinct history of a heavy fall on that hand, the elbow being extended. In the other case, the history shows that the patient slipped on the ice in such a way as to fall backward and toward the injured side. He had on his overcoat and his two hands were in the pockets of the overcoat. He says that when he fell his hands remained in his pockets and that he struck on his elbow. In spite of this, I believe that unconsciously he withdrew his hands from the pockets in time to break the force of the fall with one or both of them. He might have done so while his hands were in his pockets. What impresses a patient most about an injury is the pain, and in this fracture it was at the elbow, so that the attention of the patient was at once directed to that part as the one which must have received the force. The proof of the cause is in the skiagraph. (See Fig. 4.) A fall on the elbow could not produce such a deformity. Only a fall on the hand will explain it.

Of the museum specimen just referred to, Dr. Mutter furnished the following description to Hamilton:[12] "History unknown. The line of fracture seems to have passed through the neck of the left radius just at the upper extremity of the bicipital tuberosity. Union with deformity has resulted. Owing to the fracture having taken place within the insertion

of the biceps, that muscle appears to have drawn forward and upward the lower end of the short upper fragment. In consequence of this movement, the articulating facet of the head of the radius is tilted backward so as no longer to be in contact with the humerus. As a secondary consequence, the anterior edge of the radius rests permanently against the articulating surface of the humerus. At this new point of contact a new surface of articulation is seen to have been formed, while the original articulating facet is directed backward and lies at right angles to the one of more recent formation. At the inner edge of the new articulation of the head of the radius with the humerus contact with the ulna has developed another surface of articulation. The upper and lower fragments are united at an angle and the radius does not appear to have lost in length."

Mutter makes no attempt to explain the cause or mechanism of this fracture, but accounts for the deformity by the pull of the biceps. On this point Stimson says that fractures here are usually dressed in flexion, which would relax the biceps, so that the deformity could hardly be due to its contraction.

In the second specimen from the Mutter museum, of fracture of the neck, there is complete separation at the seat of fracture in the neck and there is no deformity present, the fragments being probably straightened in the setting of the specimen. There is, however, a Colles fracture in the same bone, which would seem to establish that the cause of both fractures in this specimen was a fall on the hand.

To return to the skiagraphic statistics and their importance in establishing the frequency of this fracture, I consider that fracture of the head and fracture of the neck are essentially the same injury, involving as they do practically the same part of the bone, being very frequently associated, having essentially the same difficulties in prognosis and treatment, and being due to the same cause. According to these statistics fractures of the head and neck are more frequent than fractures of the patella. But it may be said that some fractures of the patella, owing to the ease with which they can be diagnosed, would not be skiagraphed, so that their frequency is probably greater than these figures show. It is likely, however, that when the importance and obscurity of fractures of the radial head are better appreciated they will be watched for more closely and, as a result, their frequency will be shown to be greater.

Of the fractures of the coronoid process, it was said by these writers that they generally accompanied backward dislocations of the forearm bones at the elbow. This was not said of the fractures of the head of the radius. I would infer from this that some fractures of the radial head were lost in the skiagraphs of backward dislocations, or that the most common fracture of the head of the radius is the uncomplicated. I believe that both inferences will be found later to represent the actual conditions. In the 1500 fractures there were shown to be six complicated and twelve uncomplicated fractures of the radial head. Every experimental fracture which I produced was uncomplicated, except one in which there was a slight splinter broken off from the side of the coronoid process, which differs much from the ordinary fracture of the coronoid process. The force was applied to the top of the humerus in every successful specimen, regardless of its influence below. It was the radius alone that suffered every time, with the exception noted.

I have observed that the usual plate, showing a posterior dislocation, is a lateral view. If this were the rule, I am satisfied that a fracture of the head of the radius may easily be lost in many dislocations. We have only to look at the usual text-book illustration of that injury. The radial head is usually almost, and sometimes totally, obscured by the ulna and condyles of the humerus. If the forearm were in supination, the detached fragment would be posteroexternal and almost surely lost in a lateral view, because the line of fracture would not then be in the line of exposure, but almost at right angles to it. It should be borne in mind that one of the first important facts shown in the history of this fracture is that it was frequently associated with posterior dislocations of both bones at the elbow. I believe that many are still being lost in this way.

MECHANISM.

We are familiar with the important role played by falls on the hand in the production of fractures and dislocations of the upper extremity. I believe that the great majority of fractures of the radial head are due to this cause. Much more rarely they may be due to direct violence applied to the head—as from a blow, a fall on the elbow, or a gunshot wound. Von Lesser believed that it was due to forced flexion of the elbow, the anterior edge of the radial head being driven against the humerus in the depression for it just above the articular surface. The weight of evidence, however, is in favor of fracture during extension as the most frequent variety. The frequent association of it with fracture of the coronoid process and posterior dislocation at the elbow is well established by the dissected cases, and that these complications are due to falls on the hand there is little room for doubt.

The most frequent fracture resulting from falls on the hand is the Colles. The height at which the fracture of the radius will occur varies according to certain circumstances—as the variety in the strength of the bone, and the varying angle formed between the forearm and the ground at the time of the fall. If the angle is an acute one, the line of resistance from the ground passes upward out of the

forearm and through the anterior radiocarpal ligament, producing a cross-breaking strain on the lower end of the radius. As the forearm becomes more and more vertical, the line of resistance tends to leave the forearm at a higher level and thus to increase the height of the fracture. When the angle between the forearm and the ground is sufficiently near a right angle, the cross-breaking strain is lost and the chief resistance is transmitted to the elbow. If no injury occurs there and the force is strong enough some damage is done farther up, as at the shoulder or clavicle. The most frequent injuries occur in or near the joints—such as sprains, dislocations, or fractures nearby.

Since the upper row of carpal bones articulate practically only with the radius, when the resistance is transmitted to the elbow, it passes more directly through the radius, and the more severe impact there is of the capitellum of the humerus against the head of the radius. Evidence of this is seen in Ross and Wilbert's statistics. In 1000 cases, the first two series in which a comparison is made between fractures of the external and internal condyle, the external was fractured 41 times, the internal 24. We do not know that they were due to falls on the hand, but it is generally conceded that this is the most frequent cause of these fractures. In each of the first two series the fracture of the head of the radius was associated with fracture of the external condyle in 2 cases. In 1 case there was a fracture of the coronoid process, fracture of the internal condyle, and a slight injury to the head of the radius. It would appear that in this case the chief resistance at the elbow was on the inner side, probably through a fall on the ulnar side of the hand. In 1 case from the literature (Gordon, No. 42) there was, besides the fracture of the head of the radius, a Colles fracture and a posterior dislocation of the elbow, but no fracture of the coronoid process or other part of the ulna. The resistance here was transmitted almost entirely through the radius.

From a study of the anatomy of the elbow we have seen that in extension of the elbow the radial head projects backward so that only about the anterior half of it is in contact with the capitellum. The impact is therefore received by the posteroexternal portion of the radial cup, which is anterior when the forearm is in nearly full pronation, since in the usual falls on the hand that is the position of the forearm. This accounts for the frequent fracture of the posteroexternal portion of the head. The tendency of such a force to produce a posterior dislocation accounts for the frequent association of this fracture with the fracture of the coronoid process.

So far as the literature makes reference to this point, it shows that when only a part of the radial head is broken off, the detached fragment is almost invariably anterior or external; sometimes it has been described as occupying a posterior position, and sometimes internal.

Von Bergmann[39] explains the anterior position of the fragment in the usual way—*i. e.*, by contact of the capitellum against the anterior part of the head in falls on the hand. He says, however, that the external fragment is probably produced when the arm is in marked abduction at the time of the fall, thus bringing the capitellum in more direct contact with the external part of the radial cup. The experimental fractures which I produced give a much more satisfactory explanation. They show clearly that the anterior fragment, in the usual position of the forearm at the time of the fall, nearly full pronation, becomes an external one in the approximately supine position. The fragment may occupy any position between an anterointernal and a posteroexternal one. The posterior fragments referred to in the literature are probably examples of the latter. My 2 cases illustrate this change in position very well. In the first the skiagraph shows, from the position of the radius and ulna, that the forearm is approximately in supination, and that the detached fragment is external. The approximation of the fragments is very close, so that it is easily conceivable that following the accident during the excitement, immediately, or from the manipulation later, as in the attempts to make a diagnosis, the forearm was changed from the prone to the supine position. The fragment, which was anterior at the time of the fracture, became an external one by the time the skiagraph was taken.

In the second case the forearm was in the prone position when I first saw her, and when the skiagraph was taken. The detached fragment required a lateral view to show it, because, on account of the pronation, it occupied an anterior position in this case. The history showed that the violence producing the fracture was greater than in the first case (the fall was greater and the patient heavier), and the skiagraph showed a larger detached fragment and slightly greater separation and depression of it. Voluntary rotation was absent and any attempt to force it gave very much pain. All this, I take it, means that there was greater disturbance within the orbicular ligament, so that rotation of the forearm necessarily produced more disturbance than in the first case. It explains why the prone position was maintained from the time of the accident throughout the treatment, disappearing only after very vigorous manipulations at the hands of a masseur.

Why the head is sometimes broken into several fragments and sometimes the neck is transversely broken, I suppose, results from impact of the capitellum on the radial head farther posteriorly in some cases. The varying strength of the neck and head probably influences the kind of fracture somewhat.

Latarjet and Gazet[35] considered that the upper end of the shaft is more or less wedge-shaped, and that this is driven into and splinters the head, which is arrested by the external

condyle of the humerus. They produced it experimentally as follows: The head was fixed at its lower end in a vice and a blow of a mallet was struck on the cup-shaped upper surface of the radial head. This was divided into two parts, the anterior fragment being the larger of the two, and the wedge-shaped upper end of the shaft being immobilized between the two fragments. This experiment assumes that ordinarily the force is received equally over the whole upper surface of the head, whereas we have seen that in extension of the elbow only that part of the head which is anterior is in contact with the condyle.

In flexion of the elbow the head is in contact with the capitellum throughout. I have found nothing in the literature to show that the fracture may occur in that position, except von Lesser's case, in which the fracture was said to have resulted from overflexion of the elbow.

The reference in the literature to a fall on the elbow as the cause of the fracture is frequent. Both my cases believed that they struck first on their elbows, and one of Dr. Pancoast's cases of fracture of the neck was firmly convinced of it. I have already referred to this under the discussion of the frequency of this fracture. The putting forward of the hand in a fall is, I believe, a reflex act of which the patient is unconscious. When a fracture of the head of the radius results, there is great pain at the elbow immediately, and a likely conclusion for the patient to reach at once is that he struck on the elbow. In each case it was the part of the head in contact with the capitellum of the humerus that was broken off; so that if the impact of the capitellum produced the fracture it must have been by a fall on the hand. If in these three cases the cause was a fall on the hand, how many of the cases in the literature ascribed to a fall on the elbow were really due to a fall on the hand?

Why are these fractures sometimes incomplete? Bruns[4] produced it experimentally, and found it in 5 of his collected cases, 1 each by Malgaigne, Verneuil, v. Lesser, and 2 by Hodges. Sometimes the fractured surfaces were in contact, and at others they diverged from each other by a considerable cleft, rendering the head more prominent and, therefore, more easily palpable. In some of these there were several lines of fracture dividing the head into several fragments, each remaining attached to the shaft below. In Verneuil's case there occurred a T-shaped fracture, one line going transversely through the middle of the cup-shaped articular surface, dividing the head into an anterior and a posterior half. The other fissure was perpendicular to the first and divided the anterior half into an outer and an inner fragment. All three fragments were in contact with each other, the lines of fracture extending about 1 cm. deep into the bone. In a similar manner there occurred in one of Hodge's cases a complete, and an incomplete fracture which was also perpendicular to the first.

The incomplete fracture which I produced experimentally (Specimen VIII) showed that in that specimen at least it was simply a question of the degree of force employed and of the resistance of the bone. I have detected its presence in none of the skiagraphs I have examined, although I have suspected its presence in a few of Dr. Pancoast's skiagraphs, nor have I found any reference to it by others as being shown by the *x*-ray. I believe that a single incomplete line of fracture would almost surely be overlooked by the *x*-ray, unless the line of fracture passed through the head in almost a straight line and the direction of the rays was in the line of fracture. If there was marked divergence of the fragments its detection ought to be easy, but I think that such a condition will be very rare.

DIAGNOSIS.

The greatest need in connection with these fractures is an efficient method of diagnosis by the clinical signs. With intracapsular fracture of the neck of the femur, our greatest difficulties are associated with the treatment. Crepitus is not necessary for a diagnosis of the femoral fracture, while the diagnosis of the radial fracture has never been made without it. We are not so much in danger of confusing it, therefore, with another fracture as of overlooking it, or of calling it a contusion or sprain. Stimson diagnosed one of his cases as a fracture of some part of the external condyle, and discovered the fracture of the radial head when he excised it later. The frequency with which fracture of the external condyle is associated with fracture of the radial head, would make the elimination of the radial fracture very difficult in some cases of fracture of the external condyle. So in the cases of the coronoid process, from the nature of its cause, if a fracture of it is suspected, the radial fracture should be looked for carefully.

When we can localize the injury to the head of the radius the skiagrapher will very likely find the fracture if it is present, and when a skiagraph is not available the treatment will be intelligently carried out.

In all dislocations of the elbow its presence should be suspected and sought for. The posterior dislocations are most frequently associated with it, for reasons already given, and its presence with dislocations of the head of the radius alone has been noted with comparative frequency. I do not know that it has been found with other dislocations at the elbow, but I should suspect its presence whenever the injury was due to a fall on the hand.

From the literature I gather that crepitus should be expected in most cases. Von Bergmann[39] says that the crepitus, which may be noticed, even by the patient, and by the slight movement on pronation, is diagnostic; and that frequently the fragment and its mobility as well as the line

of cleavage may be felt. According to Bruns,[4] in the complete variety if the outer palpable border were broken off, one can feel it as an entirely movable piece, and besides, by pressure on it and at the same time pronation and supination, crepitation can be obtained. Stimson[41] says that the diagnosis after fracture of a small portion accompanying a dislocation, or by direct violence, is easy if the fragment is displaced to the position beside the olecranon, which it has occupied in most of the reported cases, for it can then be readily palpated.

In my first case, in which the skiagraph showed the fragment to be external, pronation and supination were tried, and at the same time a certain degree of pressure made in the effort to determine whether the head moved with the shaft, and yet no crepitus or mobility of the fragment whatever was obtained. If pronation and supination and pressure on the head will produce crepitation when the fragment is external, as Bruns says, I see no reason why it ought not to do so when the fragment is anterior; and yet in my second case, where a more determined effort was made to elicit it, none was obtained. Because of the pain the movements were, of course, limited, but they were decided enough to show that the head moved with the shaft. At the time I was anxious to know whether crepitus would have resulted from examination under an anæsthetic, but did not feel justified in availing myself of this opportunity. Since doing the experimental work, I have felt that in this second case there was a possibility of enough injury to the orbicular ligament to permit the edge of the fragment to catch in the ligament, so that forced movements might have increased the separation of the fragments. Where the local disturbances are severe, this danger is worthy of consideration.

The only explanations I have found in the literature for the difficulty in diagnosing this fracture have been, first, the suggestion of Bruns[4] that the fracture is in such a case an incomplete one, the two fragments being attached to the shaft, and, second, that of Von Bergmann,[39] that the intra-articular hemorrhage prevents the production of crepitus. Stimson[22] says, "On theoretical grounds I should hope to obtain crepitation in a case of partial fracture of the head by making pressure on the head with the finger and rotating the wrist gently."

I believe that the incomplete fractures are much more rare than the complete, in which case the explanation of Bruns is a very insufficient one. As for the intra-articular hemorrhage, where the fragments are free to move on each other, it could scarcely prevent the production of crepitus. As to Stimson's theory, it is disproven by the observations on my cases, and experimental fractures. One should not expect crepitus, but should be prepared to make the diagnosis without it. It might be asked if crepitus and displacement could not be obtained by pressure on the fragment upward and downward. It is impossible to get the tip of the finger between the head of the radius and the capitellum to force the fragment downward, and if the finger could be placed under the projecting edge of the head pressure upward would only force the fragment against the capitellum, with which it is already in contact. Movement of the fragment upward and downward is, therefore, out of the question. When crepitus and mobility are distinct as in Delorme's case, No. 36, the diagnosis is easy. If the fragment is freely movable it indicates that the orbicular ligament is probably torn, releasing the fragment from its grasp.

The cases in which the diagnosis can be made from increased prominence of the head I believe will prove to be, in most cases at least, fractures of the neck with tilting of the head, which have already been referred to under frequency. (See Fig. 4.)

In the great majority of these fractures not complicated by other injuries at the elbow, the orbicular ligament will probably be untorn. In one case from the literature (Adams') the capsular ligament (probably orbicular) was torn slightly posteriorly, and a portion of the head lay in the opening. There was no other fracture, nor a dislocation at the elbow. The violence at the elbow, however, was probably unusually severe in this case, since the man died forty-eight hours after the injury, and he suffered from a simple fracture of the right femur, a compound comminuted fracture of the left femur, and a laceration of the scalp. In most cases in which the fracture of the radial head is associated with other severe injuries they will be found in or near the elbow, and the chances of an intact orbicular ligament will be correspondingly less. In Bruns' 21 cases collected from the literature, there were only 5 uncomplicated. He argued that this number did not give the actual relations as to frequency, because the simple uncomplicated fractures easily escape notice owing to the insignificant symptoms produced.

In one of my experimental fractures, although the orbicular ligament was untorn, crepitus could be elicited, but in that case the line of fracture was almost straight. An untorn ligament, therefore, does not of itself prevent crepitus; it merely helps in doing so. If the line of fracture were wedge-shaped and the ligament was torn in the region of the detached fragment, the head with the fragments well approximated might still move freely without mobility or crepitus, as was shown by repeated trials with the experimental specimens. If, especially with a straight line of fracture, the fragment was once pushed away from its fellow and then replaced crepitus might be obtained. An untorn ligament, therefore, in such a case prevents crepitus only by preventing separation of the fragments.

While crepitus is a positive symptom if localized to the head of the radius, it is not essential in the average case. The symptoms in my second case were almost the exact

counterpart of those which I had observed in the first, but could not interpret.

What evidence have we upon which to base a diagnosis? Since the localized pain is a very important symptom, the patient should not be anæsthetized. The swelling will be only moderate in comparison with the pain and impairment of function, and will be most marked on the outer side of the elbow. Exclusion of fracture of the olecranon, shaft of the ulna, shaft of the radius and the condyles of the humerus can usually be made without great difficulty. The head of the radius is so superficial that tenderness of it can be localized very easily by pressure with the tip of one finger. All movements of the parts will be limited, but pronation and supination will be much the more painful, and voluntary rotation may be impossible. The history of a fall on the hand is strongly suggestive. I should consider any serious fall forward very suggestive, because I think that the hands are put forward instinctively to save some more important part of the body, which the patient may be thinking of at the time of the fall.

To recapitulate, let us suppose a patient who gives a history of a severe fall on the hand is suffering from great pain and disturbance of motion at the elbow, the disturbance affecting very markedly pronation and supination and to a less extent flexion and extension; if the pain and tenderness are very severe and distinctly localized to the head of the radius, and are much aggravated on rotation of the forearm, the patient on account of the pain finding it practically impossible to perform these movements voluntarily; and if finally fracture of the humerus, ulna and shaft of the radius can be excluded, then I believe that the existence of fracture of the radial head is more than reasonably assured. Both of my patients presented this picture very faithfully, and I think that it is a common one when this fracture is present.

I am very much indebted to my chief, Dr. A. C. Wood, with whom I have consulted frequently during my work on this subject, for the privilege of referring to an example of this fracture which came under his care about the latter part of last May. Dr. Wood made the diagnosis on the above symptoms, in the absence of crepitus and deformity. I had the privilege of examining the patient before the skiagraph was taken, and agreed with his opinion. The skiagraph showed a distinct fracture of the radial head. I was particularly gratified to be able to study this case, since it shows that the above symptoms were quite sufficient for diagnosis in his patient and my own, which I consider average cases.

Such a diagnosis is a much more rational one than is made in the average case of fracture of a rib, where crepitus, mobility of the fragments and deformity are absent. The diagnosis in such a case is made on the history of the accident, localized pain and tenderness, and pain on respiration. In such a fracture of the rib, the presence later of palpable callus is considered pathognomonic; why not the invariably consequent limitation of motion in fracture of the radial head? In fracture of a rib we are comforted by the fact that the possible confusion with a contusion exposes the patient to no danger, since the treatment of the two conditions is the same, putting that side of the chest at rest by adhesive strapping. So in a contusion or sprain near the head of the radius, the best treatment would be to put the part at rest, at least long enough to eliminate the possibility of fracture. If the joint should become freely movable without marked pain in a week, then I think fracture can be safely excluded.

Not only, therefore, is the danger of a mistake small in these cases of suspected fracture of the radial head, but we are in no danger of evil consequences from such an error, if the diagnosis of fracture be made and the treatment for it be carried out. A skiagraph should always be taken, if available, for confirmation and to show the exact kind and position of the fragments, but in the absence of such an opportunity, I think that the diagnosis can be made in the great majority of cases with safety.

On the other hand, if the fracture of the head is overlooked and the condition is treated for a contusion or sprain, the movement of the joint which is so often encouraged or forced may lead to failure of union and, perhaps, serious permanent limitation of motion in the joint.

When the fracture of the radial head is associated with other severe injuries nearby, as dislocation or other fracture, the diagnosis becomes much more difficult. The marked swelling, diffused pain, particularly on motion of the part, and the associated deformity, crepitus, and abnormal mobility prevent in a great measure localizing the signs of fracture to the head of the radius. Yet a careful examination may enable one to do so. In the presence of other severe fractures, that of the radial head is only of secondary importance. The skiagraph ought to show it unless it be an obscure plate, or the exposure be made in an incorrect plane. A suspicion of the fracture ought to be a sufficient hint to the skiagrapher to eliminate these causes of failure.

PROGNOSIS.

Since the superior radioulnar articulation will be involved in every fracture of the head of the radius, pronation and supination must always suffer; and as no movements of the upper extremity are more essential to the full use of the hand, the loss of them is a very serious matter. The line of fracture necessarily invades the upper cup-shaped surface of the head, so that flexion and extension will always be disturbed. The prognosis, therefore, in an uncomplicated case will depend upon the degree of injury to the head and

the kind of healing that follows. An intact orbicular ligament tends to keep the fragments together, so that with a sufficient blood supply through the reflected fibres of the capsule and the periosteum, and with immobilization of the joints, union of the fragments will very likely result. An intact ligament tends to prevent the formation of excessive callus on the circumference of the head by leaving no space in which it can form. When the fragments fit snugly against the capitellum of the external condyle, there is no room for the encroachment of callus in that direction, except at the margins of the cup where the approximation is less close. The inner margin of the head fits snugly in the groove between the capitellum and the trochlea, so that excessive callus cannot form at that point; but if only a slight amount formed at the upper margin of the circumference or on the sides, anteriorly and posteriorly to this point, the head could no longer rotate until the obstruction had been worn away sufficiently, or the orbicular ligament had yielded enough to permit the irregularities to glide over each other. Even if callus did not obstruct the movements, the affected serous surfaces would develop adhesions to the adjacent bone and ligament. These adhesions with the slight excess of callus which is probably always present, very likely, account for the restriction of motion which is invariably present when the splints are removed. If the fragments are firmly united this ankylosis will disappear under persistent passive movements.

Since this is always an intracapsular fracture, the synovial fluid will find its way between the fragments. It seems, however, to offer little difficulty in the uniting of the fragments when they are closely approximated, and immobilization is provided. What little fluid finds its way between the fragments is probably soon crowded out by the new tissue which is formed.

In a simple uncomplicated fracture, therefore, in which crepitus and deformity cannot be detected, or crepitus is elicited only with difficulty, the prognosis as to union and ultimate full return of function is very good, under proper treatment. Indeed, such a result has probably often occurred without treatment.

Failure to immobilize the joint may lead to failure of union, and a more persistent effort on the part of nature to develop adhesions to surrounding structures and perhaps excessive callus. Gordon's case, No. 42, is a good example. A month after the accident there was distinct crepitus over the head of the radius, but the skiagraph showed only fracture of the neck. The excision of the head showed the injury to consist of an ununited fracture of the head and neck, with one fragment of the head ankylosed in the lesser sigmoid cavity of the ulna. At the time of the operation the position of the elbow was bad, and the joint immobilized. As the fracture of the radial head was not diagnosticated until a month after the accident and no mention is made of the treatment, it is very likely that the joint was not thoroughly immobilized by the treatment. If such a fracture is recognized soon after the accident and complete immobilization provided during the healing process, I believe that ordinarily firm union will result. Firm limitation of motion at the end of a month will occur in any case, and in any position is bad, although it is worse in some positions than in others. I believe that there has been too great a tendency to resect the head in these cases.

In Gordon's, No. 42; Gross', No. 11, and Pinner's second case, No. 27, one fragment became ankylosed into the lesser sigmoid cavity of the ulna. Gross' was obtained from the dissecting room, was therefore without history, and apparently an uncomplicated fracture. Pinner's was in the Pathological Institute at Freiberg. No history was given and no other injury referred to. We can only assume that they were not recognized during life and therefore were not immobilized. In Pinner's case a false joint had formed between the fragments by eburnation of the fractured surfaces. Since, as Gross says in his case, only a portion of the head had become united with the contiguous border of the ulna, there must have been motion between the fragments or pronation and supination were lost. It is probable that the former condition existed, and, therefore, a false joint, for if the whole head was immobilized it is very likely that this fact would have been mentioned. We have, therefore, in these cases excellent proof of what motion in the joint may lead to; failure of union, and, in that case, perhaps permanent impairment of function. The treatment, therefore, in a large measure determines the prognosis.

On the other hand, in Bennett's, No. 35, and in Hodge's first case, No. 6, the specimens which were found in the cadaver, showed firm union with practically no deformity in each. In Bennett's there is just as much reason for believing that immobilization was not provided as in the above cases, judging from the lack of history and the absence of complications; and yet there was firm union without deformity, which, I think, implies good function of the joint. The fragments were probably so closely approximated by an intact orbicular ligament and the movements so limited by pain as to lead to firm union in good position. In Hodge's case there was associated a fracture at the junction of the upper and middle thirds of the radius united in bad position. The immobilization for this fracture, which was probably recognized and treated, would provide in a great measure the necessary rest for the probably unrecognized fracture of the head.

TREATMENT.

There is very little in the literature to guide us in the treatment of this fracture, and that is very unsatisfactory. Stimson[41] says: "The treatment is not so clear. One of

my cases regained good use of the joint without operation; another did the same after a primary excision; the third and fourth had completely lost rotation, and preserved only 20 to 40 degrees of flexion and extension at the end of four and five weeks, when I removed the reuniting fragments. The removal considerably improved the condition."

According to Brewer,[42] "in these cases the treatment should be open incision, thorough inspection, and removal of any fragment of bone. Excision of the head of the bone may be required if there is much comminution."

Von Bergmann[39] says: "Fixation for two weeks in any of the ordinary splints suffices for this fracture. It is better, however, to remove the splint frequently and carry out moderate movements."

The methods of treatment that have been employed, therefore, are few, and may be divided into the non-operative and operative, the latter consisting of excision of the head, and excision of the detached fragment. I am familiar with the treatment and the results in five cases, in none of which was operation done, and in every one of which was the result as good as the best obtained after operation, so far as I can learn from the literature.

The question of chief importance to decide, in my opinion, is whether motion of the head shall be permitted during the healing process. It has already been shown that union of the fragments and good function will probably often result in spite of moderate movements, and, perhaps, vigorous motion, during the process of union. The danger of non-union will, however, always be present, and if one fragment becomes adherent to the adjacent ulna or orbicular ligament serious impairment of function will result

One is tempted very much to move the joint at each dressing. A certain degree of motion is usually possible without pain soon after the fracture is produced, and in view of the intra-articular nature of the fracture the possibilities of resulting ankylosis are ominous. A fracture, however, will not cause permanent limitation of motion because it enters a joint. It has already been shown that in the longitudinal fracture of the radial head, there is little room for excessive callus formation, and usually little or no deformity from displacement of the fragments.

In the usual uncomplicated fracture, with firm union of the fragments, I should have little concern for the ultimate use of the joint. In the future I shall aim at obtaining union of the fragments first and motion of the joint afterward; and to obtain union I consider it safer to immobilize the joint thoroughly for three or four weeks, permitting no motion during that period. If the fragments were widely separated, operation would probably be necessary for the removal of the fragment or of the whole head. This would be determined by the skiagraph or by free mobility of the small fragment.

The progress of my cases in the hands of the masseur was impressive, particularly to the patients; but the physician should not lose sight of them during this period. When the splint is removed the limb will be well-nigh useless. In about three or four weeks of the masseur's treatment, both patients were able to perform ordinary light household duties. During the first two weeks in both the progress was rapid, after that it was appreciably slower, and soon it was difficult to detect it. The masseur observes this and increases the force in his efforts to show progress, and the sufferings of the patient become intolerable. At this point my first patient refused to take further treatment, the second showed evidence of great suffering, an area of ecchymosis appearing above the internal condyle, and she complained that she could not sleep on account of the pain. The elbow was considerably swollen. She was therefore advised to stop the masseur's treatment, and to depend on ordinary use of the joint for further improvement, or rather to favor that arm with the work whenever only one arm was necessary. The progress was satisfactory. The masseur's treatment had the distinct advantage of rapidly making the injured arm useful, and thus favoring and encouraging further exercise of it by the patient. When motion is used after the splints have been removed, it should be gentle at first.

It was evident in both cases that while the limitation of pronation and supination at first was more marked than that of flexion and extension, the return of the rotating movements was much the more rapid. I would explain this on the fact that rotation occurs within an osseoligamentous ring which will accommodate itself to a moderate irregularity in the radial head. After union has occurred and adhesions have been broken up there will be little to obstruct the sweep of the head in rotation.

The approximation of the upper cup-shaped surface of the head to the capitellum is scarcely as close, especially at the border of the head. There is frequently also a slight depression of the detached fragment, from the force which produced the fracture, so that irregularties on the upper surface more readily develop and lead to more stubborn limitation of motion. The approximated articular surfaces are bony, so that the obstruction in flexion and extension will yield more slowly to the forcible movements of the masseur. It has seemed to me that the adhesions are first broken up and the soft structures are compelled, so far as they may, to accommodate the somewhat changed shape of the head; and that the slow wearing effect of constant use is more satisfactory than the forcible movements in overcoming the obstruction of bone against bone. Further observation must decide this question.

A study of the results in the two cases of fracture of the head and neck is not without interest. In one, about ten days or two weeks after the accident, the patient placed

himself under the hands of a masseur. I do not know how forcible were the movements employed, but they must have been forcible enough to prevent union if the fragments were separated. The upper end of the shaft was, therefore, very likely impacted into the head, so that movement of the fragments on each other did not occur. Before the patient had placed himself in the hands of the masseur, he had consulted a good surgeon, who had suggested that the head of the radius be excised. The patient is a very successful dentist in this city, and the return of function is so nearly perfect that he experiences little or no inconvenience in his work.

In the second case, immobilization, so far as I can learn, was provided for about four weeks. At the end of that time the splints and bandages were removed and hot baking tried twice. The patient was then told to go to work and use the arm as much as he could. He could do little for about six weeks, but with the gradual increase in function the progress became more rapid, until practically full function returned. The result is somewhat better than in the first case.

From an inspection of the skiagraphs in these fractures of the head and neck, one would wonder at first how rotation could occur in the presence of so much deformity. A study of the deformity, the anatomy, and the normal movements of the parts will explain it. At the time of the accident the force which produced the fracture was applied to the anterior part of the radial head, which was driven downward and forward, making a considerable projection in front. Since the forearm was in pronation at the time, all rotation must be in the direction of supination, so that the projection on the head must sweep outward and backward against the soft tissues and not toward the ulna which would block it.

From the results in these two cases I think that the best treatment in fracture of the neck is to immobilize first until all chances for union have been taken advantage of, and to make all efforts at obtaining good function afterward. They speak strongly against the indiscriminate excision of the head.

The literature shows very few cases in which the orbicular ligament was evidently torn, and I find nothing to show how it was done. In Adams' case, No. 21, the capsular ligament was torn posteriorly and a portion of bone lay in the opening. In one of Stimson's cases, No. 34, one of the fragments of the head was displaced forward and lodged in the anterior ligament, which must, therefore, have been more or less lacerated. A considerable separation of the detached fragment as shown by the skiagraph, and free mobility of it, would be a strong indication that the orbicular ligament is torn, and unless approximation can be accomplished I think excision of the detached fragment is indicated. Such cases are probably very rare; so that the operation will be demanded in very few instances.

I have had no cases of separation of the upper epiphysis. I know of one, however, in which the physician in charge used movements during the treatment and at the end of about four weeks was satisfied that union had not occurred. Immobilization would seem to be indicated in these cases more than in the longitudinal fractures of the head, because the orbicular ligament would not have the same binding effect in the epiphyseal separation.

CONCLUSIONS.

The skiagraph is not infallible in the diagnosis of the uncomplicated fractures of the radial head. The fragments are frequently so closely approximated by an intact orbicular ligament that the line of fracture may fail to show, especially if the place is an obscure one, or the rays are directed in an incorrect plane.

If the upper extremity, in the cadaver, be disarticulated at the shoulder-joint, the palm of the hand placed on the ground, the arm held in extension and the forearm in pronation, by striking heavy blows on the top of the humerus the typical fracture of the head of the radius may be produced experimentally. The usual fracture thus produced will not rupture the orbicular ligament, and will give a detached fragment having a more or less wedge-shape, so that crepitus and deformity of the head will be absent. The intact orbicular ligament will prevent separation of the fragments, and the wedge-shape of the detached fragment will prevent movement of one fragment on the other, the efforts to produce such movement only serving to force the fragments more snugly together.

The fracture of the radial head is always partly and frequently entirely intracapsular, except for the thin attachment of the capsule to the lower edge of the fragment. This attachment probably furnishes an ample blood supply for the nutrition of the detached fragment, even if non-union occurs. Except in very rare cases, such a fragment will not become a movable body in the joint, in the ordinary sense, since the orbicular ligament, the irregularity in the fractured surfaces, and the attachment of the fragment below will prevent movement of it.

The part of the head which is broken off, in the usual fall on the hand, is anterior at the time of the fall; but, according to the later position of the forearm, may occupy any position within the arc of rotation of the forearm, which is approximately 180 degrees.

Instead of being an exceedingly rare fracture, as hitherto believed, it is a common one, its peculiarly obscure nature having rendered it especially difficult of recognition. There are more cases of this fracture, represented by skiagraphs, in the hands of a few skiagraphers in Philadelphia (55), than

the writer could find after a thorough search of the literature (48), making a total of 103.

Fractures of the neck of the radius are also common, and are usually associated with fractures of the head. They are frequently impacted, and are due to the same cause as the usual fractures of the head—*i. e.*, to a fall on the hand with the elbow extended.

Fractures of the radial head are frequently associated with posterior dislocations of the forearm bones at the elbow and with fractures of the coronoid process. In the usual skiagraph of a posterior dislocation of the elbow, showing a lateral view, the head of the radius is largely obscured by the ulna, and sometimes, also, by the condyles of the humerus; so that this fracture is probably often overlooked in such cases.

In a fall on the hand the ground acts as a resisting body. The force is from above, the momentum of the falling body being exerted through the bones of the upper extremity. In extension of the elbow only the anterior surface of the radial head is in contact with the capitellum, and as the force is transmitted to the ground chiefly through the radius, this part of the radial head receives the brunt of the force and is frequently broken off.

In an uncomplicated case, with distinct crepitus, the diagnosis will easily be made, providing ordinary care is taken in localizing the injury. Although the writer can find no case in the literature in which the diagnosis has been made during life, in the absence of crepitus and deformity, he believes that the signs are sufficiently distinct in the uncomplicated fracture to render the diagnosis reasonably easy and safe, even without a skiagraph. When available, however, the *x*-ray should always be employed. If there has been any doubt of the diagnosis at the time of the fracture, the occurrence later of ankylosis will make it positive. At the time of the accident there will frequently be a history of a fall on the hand, usually moderate swelling of the elbow, most marked on the outer side; exclusion of fracture of the humerus, the ulna, and the radius up to the neck in an uncomplicated case will be possible without great difficulty; there will always be severe localized pain and tenderness over the head of the radius, and limitation of all the movements of the elbow, more particularly of pronation and supination. Severe complications at or near the elbow may render the diagnosis difficult, but the *x*-ray, if properly taken, should settle the question.

In an uncomplicated fracture the prognosis after proper treatment is usually good and full function of the elbow may be expected ultimately. In severe complicated fractures and those treated improperly serious permanent impairment of movement in the elbow-joint may result.

When only the radial head is fractured, primary excision of the head should not be done. Excision of the head under any circumstances, even excision of the detached fragment, will rarely be required.

Union of the fragments will occur in many cases, even if moderate movements of the elbow be encouraged during the healing process. The possibility of non-union, however, will always be present, and as it will be difficult to determine the exact conditions existing within the joint, it will probably be best in all cases to permit no movement for the first three or four weeks. Movements during this period probably do little good and may do much harm.

In any case, the limb will be practically useless when the splints are removed, but in some cases the limitation of motion will be more stubborn than in others. In ordinary cases this will disappear largely in a few weeks, especially in the hands of a good masseur. After three or four weeks of the masseur's treatment ordinary use of the limb will render it gradually more and more useful, and finally in most cases lead to a full return of function.

BIBLIOGRAPHY.

1. Gant. Science and Practice of Surgery, 1878, vol. i. p. 642.
2. Berard. Diction. de méd., 1835, en 30 vol. t. ix. p. 228.
3. Ashhurst. Principles and Practice of Surgery, 1893, p. 283.
4. Bruns. Centralblatt f. Chirurgie, 1880, vol. vii. p. 353.
5. Ross and Wilbert. Philadelphia Medical Journal, December 29, 1900.
6. Velpeau. Annal. de Chirurgie, 1843, t. ix. p. 100.
7. Malgaigne. Traités des fract. et des luxat., tome i. p. 582.
8. Ibid., tome ii. p. 651.
9. Verneuil. Jarjavay les fract. des articulations. Thèse, Paris. 1851, p. 81.
10. Hodges. Boston Medical and Surgical Journal, 1877, p. 65.
11. Flower. Holmes' System of Surgery, second edition, vol. ii. p. 791.
12. Hamilton. Fractures and Dislocations, fourth edition, Philadelphia, 1871, p. 271.
13. Gross. System of Surgery, Philadelphia, 1859, p. 181.
14. Gurlt. Handbuch der Lehre von dem Knochenbruchen, ii. Theil, Berlin, 1865, p. 180.
15. Weichselbaum. Virchow's Archiv, Bd. lvii. p. 128.
16. Von Lesser. Deutsche Zeitschrift f. Chirurgie, Bd. iv. p. 202.
17. Bryant. Bryant's Practice of Surgery, 1876, second edition, vol. ii. p. 389.
18. Adams. Transactions of the Pathological Society, London, 1871, p. 205.
19. Hnter. Verhandl. der Deutschen Gesellschaft f. Chirurgie, V. Kongress, 1876, p. 39.
20. Trélat. J. de méd. et chirurg. prat., 1877, p. 157.
21. Pinner. Zeitschrift f. Chirurgie, 1884, xix. p. 74.
22. Stimson. A Treatise on Fractures, 1883, p. 433.
23. Roberts. Polyclinic, Philadelphia, 1885-86, vol. iii.
24. Moullin. Transactions of the Pathological Society, London, p. 242.
25. Wainwright. Transactions of the Clinical Society, London, vol. xx. p. 73.
26. Stimson. New York Medical Journal, November 24, 1888.
27. Bennett. Transactions of the Royal Academy, Ireland, 1890, vol. viii. p. 402.
28. Cheyne. British Medical Journal, March 7, 1891.
29. Delorme. Gazet. des hôp., Paris. 1891, lxiv. p. 296.
30. Stirling. Australasian Med. Gaz., 1891-92, No. 11, p. 98.
31. Stimson. New York Medical Journal, January 30, 1892.

32. Jayle. Bull. Soc. anat. de Paris, 1893, 5 s., Tome vii. p. 45.
33. Gordon. Dublin Journal of Medical Sciences, 1897, p. 388.
34. Stimson. Annals of Surgery, 1898, vol. i. March and April.
35. Latarjet and Gazet. Lyon méd., 1903, vol. ci. p. 405.
36. Banks. Journal of the Association of Military Surgery (U. S. A.), June, 1905.
37. Helferich. A Treatise on Fractures and Dislocations.
38. Ross and Wilbert. Philadelphia Medical Journal, June, 1899.
39. Von Bergmann. System of Practical Surgery (W. T. Bull), vol. iii.
40. Ross and Wilbert. Philadelphia Medical Journal, October 4, 1902.
41. Stimson. Fractures and Dislocations, 1899.
42. Brewer. Text-book of Surgery, 1903.

SCOPOLAMINE-MORPHINE ANÆSTHESIA.

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My attention was first directed to scopolamine-morphine anæsthesia by Terrier's excellent article in *International Clinics*, vol. ii. 1905, and on looking up the literature of the subject and finding that the reporters were almost unanimously unstinting in their praise of its virtues, I determined to give it a trial. Scopolamine was extracted by Schmidt from the Scopolia Japonica plant in 1890. Its uses have been as a sedative for the insane and as a mydriatic by ophthalmologists in a solution of $\frac{1}{10}$ to $\frac{1}{5}$ per cent. In 1900 Schneiderlin combined it with morphine and used it to produce general surgical anæsthesia, but it does not appear to have met with favor until 1903, when numerous German surgeons began to use it and published their results. Terrier[1] collected in all 1488 cases of its use, not including his own 26 cases, to which number can be added 72 cases of Ries,[2] 11 cases of Wood's,[3] 10 cases of the writer's, and 65 cases of Seelig's,[4] the latter cases, however, being only a single injection of scopolamine hydrobromate, gr. $\frac{1}{100}$, and morphine sulphate, gr. $\frac{1}{6}$, given one-half hour before general anæsthesia was induced by ethyl chloride. Scopolamine hydrobromate (Merck), from the *Scopolia atropoides*, occurs as colorless hygroscopic crystals, soluble in about four parts of water, fifteen parts of alcohol, and only slightly soluble in chloroform or ether. The maximum dose is given as $\frac{1}{200}$ of a grain per diem. It soon deteriorates and only a fresh solution should be used. Physiologically its action is said to be very similar to hyoscine, and the observations of Ries are confirmatory of these views, as he obtained precisely the same results by means of hyoscine and morphine as he did later with scopolamine.

In my cases I followed the technique of Terrier, giving scopolamine hydrobromate, $\frac{1}{64}$ gr.; morphine sulphate, $\frac{1}{6}$ gr., and aqua destil., ɱxv hypodermically four hours, two hours, and one hour before operating, and even in my small number of cases I was struck by the different way in which the patients were affected by giving the same amount to each one (except in Cases IV. and IX.), and not allowing for the differences in temperament. It would seem that women require less than men, as is true of any anæsthetic, and that highly excitable, nervous patients and alcoholics would need larger doses. In this we must be guided by the pupils, pulse, and respirations, giving more scopolamine if the pupils are contracted, more morphine if they are dilated, up to the maximum dose. After the first injection the patient becomes slightly excited, and may toss around in bed or try to get up, but soon succumbs to the increasing drowsiness, and in a quarter to half an hour is sound asleep. The pulse rate falls at first and then rises; the respirations are quiet. At the second injection the patient may rouse up and make some movements of the arms or legs, but is unconscious of the needle, and sleep becomes deeper. At the third injection anæsthesia should be complete, the skin dry and warm, face flushed, pulse regular and strong, but rapid (100 to 120), respirations slow and quiet (12 to 16), pupils slightly dilated or midway between contraction and dilatation, conjunctival reflex present. (In two of my cases there was a divergent strabismus.) It is important to remember that the patient can easily be aroused by shaking or loud talking, so that it is well to place pledgets of cotton in the ears, cover the eyes, and preserve silence in the operating room. When making the skin incision or during the operative procedures the patient may move slightly, necessitating some restraint, though the analgesia is complete, so that the operator, having his first experiences with this form of anæsthesia, may order chloroform or ether to be given when it is not necessary. After the completion of the operation the patient is carried back to bed, where he sleeps peacefully for several hours, awaking as from a natural sleep, with no nausea, thirst, or acute postoperative pain. The urine is normal. When, either through some instability of the preparation of scopolamine, morphine used, or some idiosynerasy of the patient, sufficiently deep anæsthesia is not produced by it for the

[1] International Clinics, 1905, vol. ii.
[2] Annals of Surgery, August, 1905.
[3] Personal communication
[4] Annals of Surgery, August, 1905.

performance of the operation, a very small amount of either ether or chloroform will be required. Briefly the writers cases were as follows:

Case I.—T. R., aged twenty-seven years, white, male, rather nervous disposition. Physique good. Operation August 14, 1905. Partial excision of right elbow for compound fracture and dislocation. Directly after the first injection patient became excited, pupils dilated, pulse rapid. The second injection made him stuporous with still further dilatation of the pupils; he seemed conscious of his surroundings. After the third injection he fell into a deep sleep, from which, when aroused, he became excited, muttering incoherently and moving his arms about. Moving him to the operating table further aroused him, and chloroform, ℥ij, was given. Time of operation forty minutes. Patient slept for two hours after his return to bed and awoke confused and nervous with no remembrance of being removed from the ward to the operating room. There was no nausea and the patient had a good night.

Case II.—C. Z., aged forty-seven years, white, male. Robust physique, but run down by his illness. Operation for repair of urethra. After the first injection patient became nervous and excitable, pupils dilated, pulse quickened, respirations 16, dozing for short intervals and awakening with a start. After the second injection face became pale and pulse dropped to 44, going up to 70 in a few moments, and from this time his mind was a perfect blank until two hours after the operation, when he awoke with normal pulse and respirations; no pain or nausea. As the patient moved about in the lithotomy position chloroform, ℥iss, was given to keep him quiet. Time of operation twenty-five minutes.

Case III.—C. G., aged twenty-seven years, colored, female. Tall, well-nourished woman in good general condition. Operation: excision of large carcinomatous mass of glands from the neck. Patient became drowsy immediately after the first injection, which increased with the second; pulse slightly accelerated; respirations 14. After the third injection sleep was profound; pulse slowed down to 75; respirations 14; pupils dilated; eyes in position of external strabismus. The patient moved slightly at the first incision and a whiff of chloroform was given. During the rest of the operation patient remained perfectly quiet, awaking two and one-half hours later, with no pain or nausea, soon falling asleep again and sleeping peacefully all night. Time of operation seventy-five minutes.

Case IV.—E. C., aged ten years, white, female. Small, rather anæmic child. Dose given: scopolamine hydrobromate, gr. $\frac{1}{128}$; morphine sulphate, gr. $\frac{1}{12}$, three hours and twenty-five minutes, and repeated one hour and twenty-five minutes before operation. Operation: tendon transplantation. After the first injection the child became excitable, wanted to get out of bed, then would lie down and doze for a few minutes. Pupils dilated; pulse 120; respirations 18. The second injection quieted her, but she could still easily be aroused. While she did not make any sound, she moved so during the operation that chloroform, ℥ij, was given. Deep sleep followed for two hours, when she awoke with no pain but a slight feeling of nausea. Time of operation thirty-five minutes.

Case V.—T. M., aged fifty-five years, white, male. Large bony development, with poor musculature and anæmic. Operation: stretching sciatic nerve and Bassini's operation for radical cure of hernia. Patient remembers nothing after the first injection, immediately falling asleep. Face flushed; pulse 90; respirations 16; pupils dilated and turned up. Slept for more than three hours after operation and did not have any pain or nausea on awakening. Nerve was stretched with ease, but turning the patient over woke him up and it was thought best to give him some chloroform to keep him quiet (℥iv). Time of operation, nerve stretching, ten minutes; Bassini, sixty-five minutes.

Case VI.—T. McG., aged fifty-eight years, white, male. Large plethoric man, with a mitral regurgitant murmur, good compensation. Operation: excision of lipoma of the left buttock, size of child's head. After the first injection face became very flushed, respirations quiet, pulse went up to 100, and patient fell into light sleep, which became deeper with the succeeding injections; until after the last one he could not be aroused to answer questions; he would, however, make an effort to turn himself over or give a grunt. He moved slightly when the first incision was made, and after that lay quiet. He slept for one and one-half hours after the operation, and awoke in a dazed, confused condition, which lasted for an hour or more, but he was perfectly quiet and free from pain or nausea. Time of operation fifteen minutes. In this case hemorrhage was quite profuse, due doubtless to plethoric condition of patient as much as to effect of drug.

Case VII.—D. S., aged thirty-nine years, white, male. Patient used alcohol freely. Operation: ligation and excision of external hemorrhoids. Patient seemed to be entirely unaffected by the first injection; the next two made him stuporous and dazed, though not actually asleep. Stretching of the sphincter ani aroused him to such an extent that he could not be satisfactorily controlled without further anæsthesia, so chloroform, ℥iv in all, was given. On his return to bed directly the effects of the chloroform had passed off, he became actively delirious, tore his dressings off, and was with difficulty kept in bed. He was very confused in his talk and complained of pain at the seat of operation. Delirium continued for ten hours and he was given sodii bromidi, gr. xxx; chloral, gr. xv, and morphine sulphate, gr. $\frac{3}{8}$, which finally induced sleep, lasting all night. In the morning he remembered nothing about his behavior. His pulse was good throughout, and I have seen precisely the same con-

dition in a hard drinker who was given hyoscine. Time of operation fifteen minutes.

Case VIII.—P. H., aged nineteen years, white, male. Small, well-nourished boy of average development. Diagnosis: varicocele. Operation: excision of veins. First injection caused some slight excitement; pupils dilated; pulse 110; respirations 14. The next two doses made him sleep soundly. There was divergent strabismus. Patient moved legs at first incision and then lay motionless. On the completion of the operation I roused him and asked him how he felt. "Very well," he said, "but I cannot see right." Two hours after the operation he asked the nurse when it would be performed. He slept well all night and had no pain or nausea. Time of operation forty minutes.

Case IX.—A. S., aged twenty-two years, white, female. Poorly nourished, phthisical-looking subject. Operation: incision and curettement of broken-down cervical lymph glands. (Operator, Dr. J. A. Van Kaathoven, chief resident physician University Hospital.) Before first injection, which was given two hours before operation, pulse was 56; respirations 16. After the first injection almost immediate drowsiness, more pronounced after the second and last dose, one hour before operating. Pulse went to 80, respirations were 8, pupils normal. Anæsthesia was not sufficient and chloroform, ℥ij, was given. She slept for about an hour afterward and had no pain or nausea.

Case X.—W. J., aged thirty-nine years, colored, male. Patient is a tall, thin, tuberculous subject, exceedingly nervous about himself. Pulse 60, respirations 20. Winckelmann's operation for radical cure of hydrocele. First injection made him nervous and next two doses produced fitful sleep. When he came to the operating room his eyes were open, pupils contracted, and he talked unintelligently if spoken to; his pulse was 120, respirations 18. He did not appear to feel any pain and lay perfectly quiet. For some time after the operation he was confused and excited, but had no pain or nausea.

The disadvantages of the use of scopolamine are that complete muscular relaxation is not secured, and that therefore it should not be the anæsthetic of choice for laparotomies or delicate operations, where the patient in the event of making a movement might seriously hinder the surgeon. Also in its present status, like all new things, it must be used with discrimination and in proper amounts, for, while no deaths have been reported as directly attributable to its use, should some fatalities occur, immediately there would be a wave of adverse criticism.

Its advantages are numerous. The patient is saved the fear of nitrous oxide gas, ether, or chloroform, the preliminary struggling of anæsthetization, the postoperative retching, vomiting, thirst and "ether back," and much of the pain. There is no risk of ether being dropped in the eyes, the mouth gag applied, or the tongue forceps used. Retention of urine does not occur and peristalsis is not interfered with. An anæsthetist is done away with. Last comes the question of expense, sufficient scopolamine and morphine for an ordinary surgical operation, costing, roughly, about two cents against ether at twenty-five cents per 100 gm. (Hospital rates.) In patients with pulmonary tuberculosis it would seem to be far preferable to ether, and in military surgery I think this form of anæsthesia should have a very general use during actual warfare on account of its cheapness, ease of administration, and small bulk.

THE FAT CONTENT OF LIEBIG'S MEAT EXTRACT AND OF WITTE'S PEPTONE.

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Recently I had occasion to consult the literature on the subject of the fat content of the extract of meat prepared by the Liebig's Extract of Meat Company (London), and also of Witte's Peptone, and was astonished at the very limited number of published analyses of these two materials I could find.

Karmrodt,[1] in 1866, stated that the organic substance of a meat extract analyzed by him (the name of the manufacturer is not given) contained 1.5 per cent. of fat. In 1881 Estcourt[2] published an analysis made by him of a sample of meat extract prepared by the Liebig's Extract of Meat Company, in which analysis he reported that the substance was free from fat. He compared this analysis with one made by himself of a spurious beef extract, sold as having been prepared by the Liebig Company, but which he believed originated in Italy and was prepared from horse meat, which contained 1 per cent. of fat. These analyses are published by Elsner,[3] and the fat content of the Liebig extract is given as 0.6 per

cent., and that of the spurious extract as 1 per cent., and the reference to Estcourt's article is given as having been published in the *Archiv f. Physiologie*, 1879, S. 39. Estcourt's article, or abstract of the article, is not contained in that journal, nor in the *Archiv f. d. ges. Physiologie* for the years 1879–1881, but the original article is published in *The Analyst*, 1881, vol. vi. p. 202. Furthermore, Elsner quotes Estcourt's analysis of the Liebig Company's extract as stating that the latter company's meat extract contained 0.6 per cent. of fat, whereas, in Estcourt's article in *The Analyst*, the fat content is put down as 0.00 per cent.

An article[4] emanating from the *Untersuchungsanstalt des hygienischen Institutes*, München, published in 1883, names the constituents which Liebig recommended should be determined in order to ascertain the quality of a meat extract, but no mention is made of a determination of fat. Denaeyer[5] gives as the result of his analysis of the Liebig Company's Meat Extract a percentage of 0.21 of fat.

While König[6] reports analyses of various peptones, including Witte's, with fat content ranging from 0.57 per cent. to 2.48 per cent. (Merck's peptone, powder = 0.61 per cent. of fat), the report of the analysis of Witte's Peptone shows the absence of fat, if we are to construe a dash under the column headed "Ether Extract" as meaning that the peptone was free from fat.

The meagreness of information regarding the fat content of the Liebig Company's Meat Extract and also of Witte's Peptone induced me to make determinations of fat in a sample of each one.

While it is practicable to sufficiently dry the beef extract at a temperature of 105° C. to permit of its being pulverized, it was found that in the operation of pulverizing friction caused a portion of the pulverized material to soften and aggregate in small masses, which were too large to warrant one's using the material for a fat extraction by means of ether. To overcome this difficulty, small portions at a time of the dried meat extract were triturated in a mortar with larger quantities of plaster of Paris* (aggregating about 25 gm.) until the weighed amount of meat extract had been so treated. The pulverized material was sieved by means of a sieve made of silk bolting cloth. Particles too large to pass through the bolting cloth were returned to the mortar and further pulverized, and this procedure was repeated until all of the material had passed through the sieve. The pulverized material was placed in a Schleicher and Schüll, fat-free, paper thimble and extracted in a Soxhlet extractor, with freshly distilled petroleum benzene, boiling between 20° and 50° C. The extraction with petroleum benzene continued during periods aggregating twenty hours in each case. After extraction the clear* extract was collected in glass dishes and allowed to evaporate at room temperature.

To obviate a source of error which might happen through the possibility of the petroleum benzene in the prolonged extraction operation dissolving substances other than fat, the residue from the petroleum benzene extract in each case (meat extract and peptone) was treated with repeated portions of about 5 c.c. of petroleum benzene until ten portions had been used. Each portion of 5 c.c. was allowed to remain one minute in contact with the residue and was then poured into a weighed glass dish in which it was evaporated at room temperature and the residue of fat weighed. In each of the glass dishes in which the original residue had been treated with repeated portions of petroleum benzene there remained a very slight residue insoluble in petroleum benzene and which did not respond to the reactions for fat.

LIEBIG COMPANY'S MEAT EXTRACT.

No. I. Twenty gm. of the moist meat extract, from a freshly opened jar in which the contents had been thoroughly mixed before removing the portion used for analysis, were dried at 105° C., mixed with plaster of Paris, etc., yielded a residue of 0.0062 gm., which corresponds to 0.031 per cent. of fat.

No. II. Twenty gm. of the moist meat extract treated as in No. I. yielded a residue of 0.0058 gm., which corresponds to 0.029 per cent. of fat.

WITTE'S PEPTONE.

No. I. Twelve gm. of the peptone powder, taken directly from the original container, placed in a Schleicher and Schüll fat-free, paper thimble, and extracted with petroleum benzene during a period aggregating twenty hours, yielded a residue of 0.0058 gm., corresponding to 0.0483 per cent. of fat.

No. II. Twelve gm. of the peptone treated as in No. I. yielded a residue of 0.0052 gm., which corresponds to 0.0433 per cent. of fat.

In reading the literature concerning meat extracts, as published in reputable journals, I encountered some facts which may be of interest to some of the readers of this article, although the matters are not especially germane to fat content of meat extracts.

*The plaster of Paris was freshly prepared by pulverizing, and then heating, selenite at a temperature of 105° C. for a period of six hours

*In one case (No. I. meat extract) the final petroleum benzene extract was very slightly cloudy. This was filtered through a small, hardened, fat-free filter, and the filter washed with petroleum benzene before evaporating the filtrate to obtain the residue.

In the popular mind, meat extracts are considered to be concentrated nourishing substances. It is needless to say that the manufacturers of these preparations are not disposed to discourage this view. As a matter of fact, they contain only the slightest quantity of nourishing material. Although the principal commercial meat extract bears the name of Liebig, he was not the originator of such extracts, nor did he ever claim to have originated such extracts. Liebig first referred to such extracts in 1847, and on every occasion when opportunity offered it is stated[7] he referred to the communication of Parmentier and Proust,[8] made in 1821, as the source of his information. Parmentier and Proust recommended it, not as a concentrated foodstuff, but as an invigorating material for wounded soldiers. Liebig, however, was the first to endeavor to put it to practical use, in which endeavor he proposed that the meat from the numberless animals on the great prairies of South America be utilized in preparing a meat boullion which could be preserved in the form of a semisolid meat extract. He encouraged the formation of a company to manufacture the extract on a large scale. The Liebig's Extract of Meat Company of London was founded under his auspices, and he permitted the company to use his name, on condition that they should sell only the extract which had been examined by him or by his delegate, Prof. von Pettenkofer. Whether, since the decease of Liebig and von Pettenkofer, an arrangement with other reputable chemists to examine the product exists, I do not know.

Bibliography.

1. Karmrodt. Zeit. d. landw. f. Rheinpreussen, 1866, S. 294.
2. Estcourt. The Analyst, 1881, vol. vi. p. 202.
3. Elsner. Praxis des Chemikers bei Untersuchungen von Nahrungsmitteln, etc., Leipzig, 1889, S. 21.
4. Archiv f. Hygiene, 1883, Bd. i., S. 511.
5. Denaeyer. Journ. de pharm. et de chimie., 1897 [6], pp. 357 and 359.
6. König. Chem. d. Menschl. Nahrungs u. Genussmittel, 1904, Bd. ii., S. 550.
7. Archiv f. Hygiene, 1883, Bd. i., S. 511.
8. Annal. de chimie et de phys., 1821, I. serie, tome xviii. p. 177.

A NOTE ON THE TREATMENT BY ELECTRICITY OF THE SECONDARY CONTRACTURES OCCURRING IN HEMIPLEGIA.

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Much of the disrepute into which electricity as a therapeutic agent has fallen with many is owing to the fact that it has been employed without due consideration of the end desired to be accomplished, and of the best form of current and method of applying which will attain that end. Examination will often show that in cases of hemiplegia, when contractures have developed, the patient's disability is not due so much to muscular weakness as to the deformity produced by them. Also, whatever the reason that in some cases they occur and in others they do not, when they do occur the deformity is caused by the overaction of one group of muscles, usually the flexors, and the relaxation of their opposing group. It is, therefore, apparent that in such a case stimulation of the overacting muscles will only aggravate the trouble. The writer has for a long time taught and practised the following method of treatment, with considerable relief in a number of cases: To relax the contractured muscles he utilizes the positive pole of the galvanic current, thus producing the state of anelectrotonus. This pole is placed successively over the motor points of the affected muscles and the negative pole, or cathode, is placed at an indifferent point, preferably the nape of the neck or over the sternum. The current is then gradually increased to a strength of from 5 to 10 milliampères, or as strong as the patient can comfortably bear, and allowed to flow without interruption for at least five minutes; it is then *gradually* decreased in strength to zero.

If the current is not gradually decreased, a condition of increased irritability, or katelectrotonus, will follow, which would defeat the desired end. It is also important that before the positive electrode is moved from one point to another the current be shut off in the method above described, to be again gradually increased after the electrode is moved to the desired point. After this the relaxed and weakened antagonistic muscles should be stimulated with a faradic current just strong enough to cause them to contract, about a dozen contractions being sufficient, remembering that too many contractions cause overstimulation, and hence weakening. This method may also be employed to prevent contractures, remembering that its use should not be begun until at least two weeks after the onset of the apoplectic seizure. Three treatments a week for several months should be given, to be followed by a rest of several weeks, to be again followed by the electric treatment, if necessary.

The writer has not seen this plan described in any of the treatises on electrotherapeutics, excepting that of Jacoby,[1] who has evidently also employed this method.

[1] "Electrotherapy." System of Physiologic Therapeutics, edited by Cohen, vol. ii. p. 176.

BOOK REVIEWS.

Weather Influences. An Empirical Study of the Mental and Physiological Effects of Definite Meteorological Conditions. By Edwin Grant Dexter, Ph.D. New York: Macmillan & Co.

The influence of meteorological conditions upon man has been a subject of speculation for many centuries. Although the "weather" at the present time and, still more so, in the past has been forced to shoulder the blame for many human ills whose origin were obscure, yet there can be no doubt that changes in atmospheric pressure, temperature, humidity, sunshine, etc., affect in no small degree the majority of mankind in general and certain individuals most profoundly.

In "weather influences" Professor Dexter has made an "empirical study of the mental and physiological effects of definite meteorological conditions," reviewing in an interesting manner the older folk lore and proverbs, and investigating the subject in the present from such available data as the influence of the weather upon the child at school, upon crime, drunkenness, insanity, suicide, and health statistics. The author has made it his task to separate as clearly as possible the primary weather influences from the secondary ones owing to the inclusion of which much confusion seems to have arisen in the past. G. W. N.

—

Clinical Diagnosis and Urinalysis. By James Rae Arneill, A.B., M.D. The Medical Epitome Series. Philadelphia and New York: Lea Brothers & Co., 1905.

This is a very complete little book for its size, and the contents have been well selected. Chapters are devoted to the blood, stomach contents, fæces, sputum, urine, and a few other subjects.

It should be valuable to the student and to the graduate who wishes to brush up his knowledge on clinical laboratory technique, without having to wade through some more comprehensive but lengthy volume. For the average practitioner doing a small amount of laboratory work, and called upon suddenly to make some, to him unfamiliar test, this manual should prove very useful.

The illustrations are numerous, clear, and well chosen.

Of course in all such work as this differences of opinion naturally arise between workers along these lines as to the respective value of certain tests, but, on the whole, the proper worth has been placed on the tests given, an exception being the presence of the so-called "Boston's Pipette Method" for albumin, which has for years been the lazy hospital interne's delight, and does not detect small amounts of albumin.

The recommendation to fix blood films in the flame of a Bunsen burner is a rash one, as attempting this has led many a beginner into endless trouble.

Hardly enough attention is given to the occurrence of eosinophilic myelocytes in leukæmia, which certainly are found oftener than is stated.

The author's method of examining the fresh sputum is a good one. The printing of questions at the end of each chapter is hardly worth the small amount of space consumed. The book, however, is recommended favorably to all who come within the above-mentioned classes. W. P.

New Methods of Treatment. By Dr. Laumonier. Translated and edited from the second revised and enlarged French edition by H. W. Syers, M.A., M.D. (Cantab.); Physician to Out-patients, Great Northern Central Hospital. Chicago: W. T. Keener & Co., 1904.

This book of 320 pages consists of eleven chapters dealing with the newer methods of treatment. The first chapter treats of nutritive alterants; in it considerable space is given the newer substances having phosphorus as their important base, and the discussion concerning lecithin, nuclein, the glycerophosphates, and cacodylates is especially interesting; the latter, with phosphoric acid, the persulphates, and other drugs, is placed by the author among the indirect alterants. The fourth chapter deals with respiratory alterants, the drugs discussed under this heading including turpentine and its derivatives, terpene and terpinol, eucalyptus, thiocol, etc.; a number of formulas are given suitable for intrapulmonary injections. The subjects of opotherapy, serotherapy, and vaccination are ably dealt with. The other chapters treating of blood, renal, vasomotor and nerve alterants, mineral medication, antipyretics and antiseptics, are all full of interesting reading. Each chapter is in reality an essay on the subject, many having been previously published in French medical journals. The book as a whole is valuable, and every one reading it will certainly find something of use to him in his daily work. E. L.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

THE DEVELOPMENT OF MODERN MEDICAL EDUCATION.[1]

By Alfred Stengel, M.D.,
Professor of Clinical Medicine, University of Pennsylvania.

One cannot stand beneath the ancient tower of Merton College, or enter the great quadrangle of Christ Church through the Tom Gate that Wolsey built, or wake the echoes in the cloisters of New College without a sense of the antiquity of these foundations and a feeling of reverence for the notable part that Oxford has had in the intellectual activities of all English-speaking people. Though our history has been so brief, the developments of city and country so rapid, and the changes in equipment of institutions so frequent, that we cannot here show such outward and visible signs of an ancient origin, the traditions of our University carry us back to the very beginning of all that is now substantial in modern learning, and those of the medical school with which we are specially concerned to-night link the present with the dark ages of science. If we survey in retrospect the history of our school and the labors of those who have made it what it has become, we shall have a picture of the development of modern medicine from the dawn of real science, and, moreover, we shall learn to appreciate the conditions that made the progress of learning so difficult on this continent.

Happily, fate so timed the origin of this University and its medical school that their infant days fell in a period of revival, a new renaissance of learning, art, and industry following an age of intellectual depression. The first half of the eighteenth century will be forever remembered as a period of profligacy in public and private life, of levity or licentiousness in literature, of political intrigue and wanton wars, of skepticism in religion and of stagnation in science and every form of learning. The Court of France, under Louis XIV. and XV., shone as a brilliant example of wasteful extravagance, of oppression of the poor and light-hearted and light-minded depravity of the nobles and of irreligion. England, through the reigns of the first two Georges and the long ministry of Walpole, was a hotbed of political corruption, and though long at peace, the peace was one of pusillanimity and dishonor; while Frederick, of Prussia, dominated Northern Europe with a military hand. One searches the history of this era almost in vain for characters that have made an impress on intellectual or material progress or for movements in the direction of the elevation of the people. The literature of the Continent was controlled by the skeptical and cynical genius of Voltaire, and that of England by the superficialities and artificialities of Pope. The brilliancy of Addison and the genius of Swift availed little to set a higher standard in England; the scholarship of Bently and the philosophy of Bishop Berkeley and Leibnitz were almost unnoticed; and even Locke's "Essay on the Understanding" and the "Principia" of Newton failed of appreciation, or even of recognition, as masterpieces of philosophy and science.

Suddenly the scene changes and the second half of the century stands out as a period of general awakening of activity in every branch of material, moral, and intellectual endeavor. It might be profitable to inquire into the causes that led to this surprising change, but for the present we are interested mainly in the results.

In England, political dishonor, profligacy, and corruption came to an end with the fall of Walpole, and gave place to the aggressive, honorable, constructive statesmanship of Pitt that roused the kingdom and left it an empire. The victory of Clive at Plassey and of Wolf at Quebec enlarged and established the Indian and American Colonies, while the steadfast and successful opposition of the minister to the pretentions of the King kept the imperial government free from tryanny and dishonor and nourished the growth of democracy.

In literature, the debasing influences of the poets of the restoration and of their successors yielded place to the refinement and love of nature of Thomson, Gray, Cowper, and Goldsmith. Even the novels of Smollet, Richardson, and Fielding were pure in comparison with the earlier standards. Throughout the second half of the century the authority of Samuel Johnson was absolute, and was ever exerted to elevate the dignity of letters.

In philosophy, Burke's essay on the "Sublime and Beautiful;" in law, the "Commentaries" of Blackstone; in political science, Adam Smith's "Wealth of Nations;" in history, the works of Robertson and Hume and the monumental labor of Gibbon marked this epoch as one of industry and cultivation.

In art, the appearance of Sir Joshua Reynolds, Gainsborough, and Romney gave a distinction to English painting that has never been surpassed; while the ovation given to Handel's "Hallelujah Chorus" touched even the King himself.

[1] Address read at the opening of the one hundred and fortieth session of the Medical Department of the University of Pennsylvania.

The rights of man and the overthrow of oppression found advocacy in John Howard's campaign for prison reform, and in the efforts of Wilberforce, Clarkson, and Pitt to abolish human slavery. John Wilke's opposition to authority and the letters of Junius were other potent influences on the side of the commoner and against the powerful and corrupt.

In religion, the fervor of the Wesleys and the eloquence of Whitefield impressed the poor of both continents and opened the way for greater toleration in the established church.

Finally, even in material industries the dawn of the new century was foreshadowed. Watt's perfection of the steam engine, Arkwright's invention of the spinning-jenny, and Brindly's construction of the first canal were among the notable industrial achievements.

Science alone lagged behind and did not receive its proper impetus until the opening of the nineteenth century.

Modern medicine was never at a lower ebb than when the House of Hanover assumed the English throne. The two great intellects of the day, Sydenham, the father of English medicine, and Boerhaave, the distinguished professor of Leyden University, from which, through Edinburgh, this University has had its lineal descent, exercised less influence upon their contemporaries and immediate followers than upon the medical men of a later day, when a rational awakening had begun. Radcliffe and Mead, Garth and Arbuthnot, the popular leaders of the profession in England, were more distinguished for their wealth and splendor, their literary culture, and their pompous domination over the lower order of practitioners, the apothecaries, than for their devotion to the elevation of medicine as a science.

The medical world was devoted to theories, unsound speculation, and mysticism that all the efforts of Sydenham and the splendid results of his logic and rational good sense had failed to check. We may smile in derision at the formula published by Van Helmont in the sixteenth century for creating mice by putting linen in a receptacle with bread and cheese; but even in the middle of the eighteenth century, Needham, the English theologian and pupil of the great naturalist Buffon, described the spontaneous generation of vinegar eels, which led the sarcastic Voltaire to write in his *Philosophic Dictionary:* "It is very strange that men should deny a creator and yet attribute to themselves the power of creating eels."

The most popular medical doctrine in England was the Brunonian system of John Brown of Edinburgh, who taught that all disease is a result of irritation, and that health itself is but an intermediate stage between the diseases due to high and low grades of irritation. Everywhere imperfectly observed facts were forced into some sort of harmony with an artificial theory, and few, if any, followed the injunctions of Sydenham to study the natural history of disease, to record observations, and to avoid theories. His belief in the power of nature to control disease, the "vis medicatrix naturæ," was derided as a foolish hypothesis. The pupil had little opportunity to see and learn in a practical way, and was indeed a froward disciple if he forgot the Aristotelian maxim, "discentem oportet credere" (the learner must believe). Hospitals were just beginning to be established: in London, Westminster was opened in 1719, Guy's in 1723, St. George's in 1733, and London Hospital in 1740; the Edinburgh Hospital was founded in 1736; the Jervis Street Hospital of Dublin in 1726; and our own Pennsylvania Hospital was begun about 1751. Notwithstanding the establishment of these houses for the sick, their utilization for the teaching of medicine was practically negligible during the early and middle portions of the eighteenth century, and the physicians of the day were well named "medici ex commentariis" (physicians educated out of books). The popular taunt that "a new physician must fill a graveyard before he can know disease" was almost merited, and is it any wonder that he embraced each new theory, however fantastic? Even the wisest were victims of the prevailing doctrines, when the learned and philosophic Bishop Berkeley could write "A Chain of Philosophic Reflections and Inquiries concerning the Virtues of Tar Water," and advocate this precious fluid for the treatment of all manner of diseases.

Such was the state of medicine through the early part of the eighteenth century and nearly down to the date of the establishment of our medical school in 1765. But a few years before Giovanni Morgagni of Padua, in his seventy-ninth year, had published his monumental work on the seats and causes of disease, as determined by anatomical investigation ("De Sedibus et Causis Morborum per Anatomen Indagatis," 1760), a work which even to this day may be consulted with profit, and which in its time was as remarkable for its scope as for its epoch-making departure from the traditions of the period. At the same time the illustrious John Hunter and his but little less distinguished brother William, the Bells, and Cullen of Edinburgh, who was the first to break the shackles of tradition and lecture in the English language, gave English medicine a new tendency by their devotion to observation and scientific method.

In Germany the tendency to realism in science was receiving encouragement and material aid from an unexpected quarter. Goethe, the great genius of German literature, in his universality of attainment, had made the natural sciences his own and had broadened their scope by the principles which his powerful and logical intellect had suggested.

In France, Bichat laid broad foundations for scientific study, objecting strongly to the prevailing tendency to speculation and even to books themselves, and insisting upon the fundamental importance of observation of facts. He claimed for medicine an exactness which had been denied it, and based his claim upon the knowledge of morbid changes in

diseased organs and the progress that had been made in diagnosis. He himself first divided the peripneumony of the ancients into pleurisy, pneumonia, and bronchitis, and his other contributions to anatomy and pathology gave evidence that his untimely death, at the age of thirty-one years, robbed the medical world of a character scarcely excelled in the annals of science from Hippocrates to the present day.

Perhaps no more fortunate time could have occurred for the institution of medical teaching in a new country unhampered by traditions and established by hardy and progress-loving settlers. The spirit that had resisted oppression in England during the previous century, and that was preparing the English colonies in America for a similar struggle, the spirit of enlightenment that makes men see their rights, as well as their duties, and that makes them strive for better things, was moulding men of lofty ideals to carry the work of advancement onward. Great men are not the accidents of stirring times; they are the finished product of the evolutionary processes that through a period of years prepare a whole people for some great movement. Our Washingtons and Hamiltons and Franklins were not sporadic growths in untilled land, but rather the most fruitful products of a long cultivation that had filled the colonies with plenty. Their pre-eminence was that of the tallest trees of a forest of sturdy oaks. Fortunately, some of the noble souls of the later colonial period turned to medicine. If culture, patriotism, far-sighted prescience of the directions of progress and scientific zeal be measures of greatness, John Morgan, the founder of this school, and Benjamin Rush, the American Sydenham and one of the first four professors of the medical school, must ever be reckoned among the distinguished figures of the Revolutionary period. In medical ability and practical wisdom, William Shippen, Jr., and Adam Kuhn, the other two of the original faculty, rank with the best teachers of any time or place.

John Morgan, born in Philadelphia in 1735, a graduate of the Academy of Philadelphia in 1757, a pupil of John Redman later the first president of the College of Physicians, a student in London under John Hunter and his brother William, completed his studies in Edinburgh in 1763, and during the two following years visited the centres of learning and the distinguished scientists of the Continent of Europe. Returning to his native land in 1765, he delivered at the commencement of the college, held May 30 and 31, 1765, "A Discourse upon the Institution of Medical Schools in America," a document that led to the immediate establishment of the medical school of this University and to his selection as professor of the theory and practice of physic. The literature of the eighteenth century contains no presentation of the foundations and scope of medical science and of the needs of systematic training and preliminary education comparable to this dissertation of young Morgan, then in his thirtieth year. Indeed, it may be said with truth that, having regard to the status of science generally, no more notable contribution has ever been made to the subject of medical education.

William Shippen, the second professor in the medical school, was elected a few months after Morgan to the chair of anatomy and surgery. Born in Philadelphia in 1736, a graduate of the College of New Jersey (now Princeton University), a student under his father, who was a practising physician, and in London of John, and especially William Hunter, he received his medical degree at Edinburgh and returned to America in 1762, after five years' study in Europe, where he had been the esteemed friend of the Hunters, Fothergill and other leading medical men of the day. He had discussed the establishment of a medical school with his friend Morgan in England, and during the three years between his own and Morgan's return to America had lectured privately on midwifery and anatomy.

Adam Kuhn, born at Germantown in 1741, a student for a time in the academy, a pupil of his father, who was a native of Suabia, he studied botany under the renowned Linnaeus in Sweden and graduated in medicine at Edinburgh in 1767. Returning to America the next year, he was elected professor of botany and materia medica, and after a service of twenty-one years was transferred to the professorship of practice.

Benjamin Rush, born on a farm in Byberry Township, near Philadelphia, in 1745, gave early promise of a distinguished career in medicine. At the age of seventeen years he translated the Aphorisms of Hippocrates and recorded some observations on the yellow fever of 1762. After serving as a pupil under John Redman he completed his medical studies at the University of Edinburgh in 1766, visited London and Paris in 1768, and returned to Philadelphia the next year. He was immediately elected to the professorship of chemistry in the College of Philadelphia, and later in the same year to the professorship of practice. In 1791, when the college was merged in the University, he was elected professor of the institutes, medical and clinical practice.

To these four young men, the youngest aged twenty-four years and the oldest but thirty years at the time of their election to professorships, the fortunes of the first medical school in America and, in a greater measure than we can appreciate, the destiny of medicine itself were entrusted. Fortunately fate had provided men who in their character, training, and disposition were worthy the great work to which she had devoted them; and luckily the awakening of interest in education and science, then manifest in all parts of the world, made the time most opportune, while the recent establishment of the Pennsylvania Hospital promised facilities for teaching that were little excelled in the oldest centres of Europe. Despite these advantages, however, the successful

development of a medical school was opposed by the unsettled state of the colonies, the primitive and hard circumstances of life, and the consequent want of preparation for higher education.

Consider for a moment the condition of the country and of Philadelphia, its principal city at that time. The population of the entire thirteen colonies was about 2,500,000 persons, white and black, and these were scattered in villages and on farms, or even in frontier outposts, so far removed from the cities that weeks passed without news or communication of any kind. Philadelphia had in the neighborhood of 25,000 inhabitants, though it was the principal city in the country. Travel was so slow and other methods of communication so difficult that later the Continental Congresses were long delayed in their meetings and in receiving ratification of their enactments, some of the members travelling weeks to reach the meeting-place. The first stage coach from Philadelphia to New York, starting from "The Sign of the Death of the Fox," reached New York in three days, and a third line, begun in 1766, was modestly termed the "flying machine," because it consumed but two days in the journey.

The city of Philadelphia in 1760 extended about to what is now known as Fifth street, and residences built at Tenth street were reached by crossing fields, their owners being derided for building fine houses so far in the country. Mr. Griscom advertised the special advantage of his academy situated in Vine street as "its position far from the noise of the city." The houses were substantial, though plain, but the streets until 1760 were unpaved and choked with mire and the pavements only marked off by posts and gutters. Down to 1751 the city was in total darkness at night, but at this time an act was passed for "a nightly watch and for enlightening the city." The houses were lighted with dipped candles in brass or copper candlesticks, though occasionally the affluent used mould candles, made at home in little tin frames. Marble mantels, folding doors, sofas, wall paper, and even carpets were unknown, and the citizens were content with whitewashed walls, white-sanded floors, large tables, and high-backed chairs. Pewter plates and dishes were in general use, and china was a great rarity. Glass tumblers were scarcely ever seen, and punch, the common beverage, was drunk from one large bowl of silver or china.

The conditions of domestic life were of a primitive sort. The most distinguished citizens lived in Front street adjoining or above their offices or shops. Food was of the plainest kind; luxuries were unknown; every housewife spun her own flax and made her own linen. Beer was a penny a pint in New York and a penny a pot in Philadelphia. Amusements, excepting those of the country, were looked upon with some disfavor, but horse-racing and bull-baiting were tolerated, and even so respectable a citizen as Dr. William Shippen, one of our early trustees and the father of the first professor of anatomy and surgery, enjoyed cock-fighting and bred game-cocks for his friends.

The best-cultured people in the community found a few volumes of hymns and sermons, the *Tattler and Spectator*, the *Vicar of Wakefield*, Fielding and Smollet, and the contemporary British poetry sufficient to supply the thirst for literary entertainment. The *Pennsylvania Gazette*, for a time conducted by Franklin, and a half-dozen other papers, most of which were discontinued after a brief life, constituted the periodical literature of the day.

Such was the state of the colony when the medical school of the University was opened in 1765, and I have detailed for you as briefly as was possible the state of learning and of medical science throughout the world when the founders of that school began their undertaking. Were we to trace the history of the institution from that day to this we should find in the teaching of successive faculties a panorama of the growth of medical science from the rude empiricism of the eighteenth century to that perfection of detail that marks the beginning of this century. Writers have spoken of the nineteenth as the wonderful century, and surely the developments in medicine have been no less conspicuous than those of the other sciences and the arts or industries.

At its very beginning we find the discovery and perfection of vaccination one of the greatest achievements of science in all ages. If it be true that the popular medical system of Brown of Edinburgh sacrificed more lives than the French Revolution, it is certainly far more likely to be within the bounds of moderation to say that vaccination has saved more lives than have been sacrificed in all the wars since Caesar conquered Gaul. And this was the contribution of a Gloucestershire country doctor, the pupil and friend of John Hunter, one therefore who had learned the value of close observation and the futility of mere speculation. It is not unprofitable for those who are about to adopt a life in which ignorance and misunderstanding will surely be encountered to reflect upon the violent opposition that Jenner and his followers suffered on every side. It is also profitable to recall that Jenner continued his observations during ten years before he published his claims to the world.

During the early years of the nineteenth century the leading spirits, guided by the example of Morgagni and Bichat and the growing tendency to more exact observation, added material facts regarding the anatomy of disease and greatly extended the scope of medical knowledge. In France, Corvisart, the incorruptible physician of Napoleon, laid the foundations of knowledge of diseases of the heart, while Laennec perfected Auenbrügger's method of physical examination and opened the way to the study of tuberculosis of the lungs. Andral and Chomel, two distinguished clinicians, devoted themselves with admirable zeal to investigation of disease in every phase, as Andral's own words attest: "I

have now," he said, "begun medicine several times from the very beginning: first, in my studies of pathological anatomy; then, through the aid of auscultation and percussion; lastly, in my physical and chemical investigation of the fluids of the body, and I scarcely think this will be the last time." How different is this from the mystical, speculative, crude, and empirical method of the preceding era. Still more does one see in the work of Louis, the greatest of the French school, the devotion to accuracy of observation. His work on the pathology and treatment of tuberculosis of the lungs was based upon the postmortem study of 358 cases and the clinical examination of 1960; while his differentiation of typhoid and typhus fevers was the result of the painstaking observations of many years.

In England, Matthew Baillie, nephew of John Hunter, continued the brilliant scientific observations of his noted uncle, and established pathological anatomy in Great Britian. Addison, the discoverer of certain peculiar diseases of the suprarenal capsule and of pernicious anæmia, and Bright, whose name must be forever associated with disease of the kidney, established Guy's Hospital on the role of medical fame; while in Dublin, Cheyne and Stokes and Graves gave a lustre to the medicine of Ireland that attracted the attention of the world.

Among German-speaking races, Rokitansky and Skoda cultivated pathological anatomy and rational internal medicine, and aided materially in raising each to the status of a science.

If we now turn to special discoveries or contributions and select those of greatest importance we shall find a succession of advances along the lines of application of exact observation and the correlated natural sciences to practical medicine. Sometimes the superficial fail to realize the importance of abstract science and its contributions. To such the discovery of the vegetable cell by Schleiden and of animal cells by Schwann must have seemed facts of no consequence; yet these discoveries were the foundation upon which Virchow raised his "cellular pathology," and, almost at a stroke, revolutionized the science of pathology. The conception of the cell as the anatomical unit, like that of a cellular function as the physiological unit, underlies the entire fabric of the medicine of to-day. With Virchow's work completed, medicine for the first time gained a glimpse of the fundamental processes of disease and was prepared for an approach to a scientific knowledge of etiology, the study of the causes of disease.

The germ theory, a favorite subject of speculation of early and even ancient philosophers and physicians, was finally established by the researches of the immortal Pasteur. Nowhere in the annals of man can there be found a more splendid exposition of the possible results of close reasoning, untiring and accurate experimentation and genius than in the writings of Pasteur on fermentation and the causes of silkworm disease. Trained as a chemist and devoted to crystallography, his interest in the crystal forms of tartaric acid led him through his study of fermentation to the final refutation of the century-old hypothesis of spontaneous generation and the establishment of the germ origin of fermentation. The solution of the microbic nature of the silkworm disease and of the infectious character of certain diseases of animals was a natural sequence in the labors of the great French scientist. The discovery of the micro-organismal causes of tuberculosis by Koch, of cholera, of typhoid fever and of diphtheria, of tetanus, and many other diseases followed quickly, and progressively the science of bacteriology was elevated to greater and greater exactness.

The time was ripe for some constructive mind to apply the results of these scientific labors to a definite practical purpose. Lister supplied this step, and by his system of antisepsis opened up possibilities in the cultivation of surgery that are too far-reaching for me to more than hint at to-night. Consider conditions within the memory of your elders in this room: hospital wards filled with cases of erysipelas, sloughing wounds, hospital gangrene, fatal infections after the most trivial operations; contrast with this the impunity with which the surgeon of to-day explores the abdominal cavity, opens the thorax, even sutures the punctured heart; and remember that all of this is the result of the practical genius of Lister.

But other factors enter into the development of modern surgery, one of which cannot be forgotten. To the American Morton, the discoverer of ether-anæsthesia, and to Simpson of Edinburgh, the first to introduce chloroform into medical practice, mankind owes the banishment of pain, and Listerism a large share of its practical applicability.

The physiologist and the chemist have been the unobtrusive agents that have made many of the great practical discoveries of modern times possible, and they were the first to be entitled to any claim among medical men to the name of exact scientists. Beginning with the discovery of the circulation of the blood by Harvey in the seventeenth century, physiology was occupied for two centuries with problems more or less roughly physical; but its growth in the nineteenth century has been quickened by the perfection of electric appliances, the development of chemistry, and the refinements of physics. Our knowledge of the chemical functions of organs, of excretions, of the localization and pathways of nervous impulses, of internal secretions, of the physiology of the special senses, all are contributions to exact knowledge that witness the ever-increasing importance of the cognate sciences, physics and chemistry. Everywhere in this field one sees the devotion of the student to exact scientific method and to facts; and be it observed as another evidence of exactness, that as rational medicine disposed of

one after another of the pretentious theories of life and disease, so physiolgy has banished much of the metaphysical jargon of the past and established experimental and rational psychology.

Finally, let me refer for a moment to new tendencies in the treatment of disease. To the physiologist must be credited the evolution of the modern pharmacologist, and in place of a botanical foundation, physiological training is now the requisite of the therapeutist. Empiricism is not yet banished, and there is a kind of empiricism, such as that which led to the discovery of the properties of quinine, that can never be wholly set aside. So long as the fundamental mysteries of life and vitality remain unknown, and perhaps these are unknowable, so long will a certain amount of empiricism be necessary, but it is of the same sort as that which utilizes the force of gravitation, though it cannot explain the essence of this force.

Even therapeutics, then, can lay just claim to a scientific character. If, to select but a few examples, the pathological and physiological investigations that led to the use of thyroid extract in the treatment of myxœdema, of suprarenal extract in shock and hemorrhage, of nitrite of amyl in angina pectoris, physostigmine in intestinal tympany, and belladonna in iritis are not entitled to rank as scientific and exact, where shall we look for exactness and science, and what are the requisites to be fulfilled? We cannot deny that much of the therapeutics of the past and present lacks this foundation, but may we not keep the best in mind and establish this as our standard?

Recently a practical outcome of bacteriology has proven a powerful stimulus to new endeavor in therapeutics. I refer to the production of antitoxins. One practical result has been to rob diphtheria of most of its terrors and to open the way to like results in other diseases.

If I have omitted references to many things that may come to your minds, such as the contributions in special branches of medical science, it is because time permits us only a general view of a field in which the details are bewildering in number. Throughout all that I have said of the medicine of this century, you will observe that one of its distinguishing traits is the abandonment of attempts at establishing comprehensive theories of disease and hypotheses to explain the very essence of life itself and the adoption of a campaign of exploration in the realm of knowable facts.

What now at this stage of medical science is the proper aim of the student who devotes himself to its cultivation? You cannot all be scientists exploring new fields, and you do not wish to be, but you must remember always that you enter into this rich heritage of knowledge and that it is yours to employ in practical ways. And if you do not contribute to the growth of science and only take it and utilize it as you find it, believe with Milton:

> ". . . Thousands at His bidding speed
> And post o'er land and ocean without rest;
> They also serve who only stand and wait."

Gentlemen of the first and second years' classes, remember this: You have not come here to learn a definite number of facts; you have come to be educated as physicians, and mere *knowledge* is not *education*. "The greatest clerkes ben not the wisest men" (Chaucer).

"What," says De Quincy, "do you learn from 'Paradise Lost'? Nothing at all. What do you learn from a cookery book? Something new, something that you did not know before. . . . What you owe to Milton is not any *knowledge* of which a million separate items are but a million separate steps on the same earthly level; what you owe is *power;* that is, exercise and expansion of your own latent capacity of sympathy with the infinite." This is the keynote of education—*power*—to see, to know, to strive in the right direction and to achieve. And to gain this power you must begin at the rudiments and master these. Some of them it is well to forget. I am happy not to be able to remember that the methylene blue which has so often stained my fingers is the methythioninæ hydrochloridum of polite therapeutic society, and that trional masquerades as sulphonethylmethanum; but your vigorous young intellects will easily recall these things at a certain time—and for a little while after. I am glad that no inquisitive professor will ask me to describe for him the organ of Corti, but I know that you will do it cheerfully and furnish a diagram besides. Are these and similar things useless? Is it useless effort that a child creeps before it walks, or is the effort a step in evolution? There is such a thing as habit of mind as well as any other habits, and training along certain lines cultivates a kind of habit that is different from others. Lawyers have their ways of approaching questions that differ widely from the ways of the clergy; men of affairs see life differently from scientists; and politicians are a law to themselves. The medical mind in its highest and best state of cultivation is a thing of a definite sort, and a highly desirable acquisition.

In your first and second years it is our duty—and we regret it as much as you—to teach you many things that do not seem immediately practical; but you will find later on that each step leads to another, and so in time you will develop this habit of mind—the scientific habit. And what is science? It is not, says Huxley, "as many would suppose, a modification of the black art suited to the tastes of the nineteenth century and flourishing mainly in consequence of the decay of the inquisition. Science is nothing but trained and organized common-sense. The man of science, in fact, simply uses with scrupulous exactness the methods which we all habitually and at every moment use carelessly."

It is this habit of scientific accuracy, and not merely certain aggregations of facts, that you must learn in your prepara-

tory years. Later on, with this habit of thought fixed upon you, you will safely observe and even speculate in the less certain field of practical medicine, where the individuality in different patients modifies processes that are fundamentally similar. The scientifically trained physician may be trusted here, as some believe the trained Republican may tamper with the tariff, though the Democrat might hasten on destruction.

Later on you will reach more practical studies, and we shall try to teach you how to observe, remembering the injunction of good old Comenius: "Let this be our business that the schools may cease to persuade and begin to demonstrate, cease to dispute and begin to look, cease, lastly, to believe and begin to know." Your first business will be to learn the use of your own senses, for the order of education ever was to train the senses, then the memory, and finally the intellect. "*Nihil est in intellectu quod non prius fuerit in sensu.*"

Of course, we shall expect you to learn a few facts, and there will be occasions when we shall inquire somewhat casually into your store of them; but the important matter is that you should learn how to ascertain facts that are before you and reason logically and scientifically from these. "It is better to know a few things and have the right use of them than to know many things which you cannot use at all." Gradually the trained physican with scientific development and cultivated powers of observation acquires a certain instinct that guides him right, even in cases in which demonstration is difficult. Medicine has been called an inexact science, and doubtless there is much that could be more exact; but when the physician has learned in general the broad outlines of infectious processes and their results, and proceeding from this basis of knowledge asserts his belief in the infectious nature of rheumatism, not yet demonstrably an infection, he follows the same scientific habit that enabled Cuvier to construct his fish from a single bone. It is this sort of training in exact scientific method that must be the fundamental equipment of every modern physician.

But there is another side to the matter. For a long time there has been in some quarters a tendency to decry that which is practical or utilitarian, and, if you please, empirical, and to exalt the scientific. Since the early days of the pathological school of medicine in France, and more markedly in the Vienna school than in any other, therapeutic nihilism has attracted attention. The practical denial of the value of therapeutic measures, because it is difficult to explain their manner of operation, is neither scientific nor practical wisdom. The fact that the natives of South America learned the value of quinine in malaria, and that we do not to this day know how it acts; that the use of iron in anæmia, mercury in syphilis, iodide of potash in syphilis and actinomycosis, opium in its relief of pain, is based upon empiricism alone, does not rob the practice of its value. Let but a trained mind accustomed to scientific accuracy of observation record and weigh the evidence and empirical knowledge approaches closely in value to that which is rigidly scientific. The nihilistic school has never found much encouragement or comfort among us here, and you will do well to avoid any temptation to subscribe to that unorthodox creed.

Another unfortunate result of excess of zeal toward extreme scientific accuracy is the tendency to make of medicine a purely objective study. Investigators in pathological anatomy and bacteriology sometimes err in regarding only the causes and the material manifestations of disease and neglecting the human subject. There is in medicine a variable factor, to use a mathematical phrase, the human being. The essence of personality, the laws of idiosyncrasy, and the reactions of different individuals or the same at different times to certain similar agencies; these are among the problems that have as yet but partial solution, and that prove the futility of purely objective medicine. You will be taught—and you will do well to consider this teaching earnestly—that the man himself is an important factor in pathology. A French pathologist has said in Gallic epigram: "One should not speak of pyogenic micro-organisms so much as of pyogenic persons." You may recognize in this some measure of return to older doctrines, but there is this difference, that a beginning has been made in the direction of determining the causes of individual susceptibility or immunity, and, further, that in these days the physician, seeing clearly *all* of the conditions in a case, and not merely a few superficial symptoms, is less and less disposed to magnify the importance of idiosyncrasy.

The untrained who see only partly the phenomena in a given case naturally find wide variations in the same diseases; while those who appreciate the whole condition are but rarely surprised by unexpected developments. Thoroughness, therefore, is a most commendable quality in practical work, and you will find abundant opportunity for its cultivation in the last two years of your study, for you will be much in the wards of the hospital. Learn there these things above all else: careful observation, system and method in your examinations, and medical memory, which will make you quick to recognize conditions seen before. Didactic lectures no longer play the part that was assigned them in earlier days. Those that remain have been selected as the indispensible minimum, and the student will find it profitable to attend strictly to these and supplement their teaching by systematic reading.

Your practical work in the hospital is not so much to give you the opportunity to see numerous cases as to familiarize you with the methods of observing them. It is method, method from first to last, and not mere facts, that we would impress upon you. The latter you will learn by reading, and

later by practical experience. "Facts," says Bacon, "have been gathered to profusion; yet this error of our profusion has become the occasion of our indigence."

It has always been the boast of this school that her alumni have been trained in the broad lines of clinical observation. It is our pride and hope to remain ever a great clinical school from which will go forth men trained in the broadest scientific spirit, endowed with a full sense of the dignity of medicine as a science, but at the same time so equipped that they shall be prepared to meet the practical problems of the physician with credit to themselves and their alma mater. We would not have you finished scientists without the method of the practical physician, nor poorly trained clinicians with neither the scientific habit of mind nor a just appreciation of the part that science plays in the every-day affairs of the doctor.

Above all things, whatever your abilities, we would have you leave these halls as men of character who will meet the exacting duties that are before them in uprightness and honor, to whom the community may look with confidence and entrust its welfare with security.

MEDULLARY GIANT-CELL SARCOMA WITH CYST OF THE LOWER END OF THE ULNA.

By Gwilym G. Davis, M.D.,
Associate Professor of Applied Anatomy, University of Pennsylvania.

The rarity of sarcomatous growths originating from the medulla of the long bones instead of the periosteum, accompanied by cyst formation and the question as to treatment, makes the following case worthy of record:

A child aged two and one-half years had an attack of tonsillitis, which subsided and was followed ten days later by a cervical adenitis which extended down the neck and involved the axilla. The temperature ranged from 100° to 105° daily for one week, and the inflammation of the glands subsided without the occurrence of suppuration. Two months later it was noticed that pain was complained of

Fig. 1.—Skiagraph showing the cyst of lower end of ulna.

when the right wrist was grasped and it appeared slightly swollen. There were no signs or history of any injury. During the next two months the swelling slightly increased, but the pain lessened to be followed in the following month by an increase both in the pain and swelling. The hand and forearm were bandaged on a splint and a dressing of ichthyol and mercury applied. Two skiagraphs were taken four months apart and showed apparently a cyst of the lower end of the ulna (Fig. 1). The swelling involved about 4 cm. tense (1½ in.) of the lower end of the ulna, was fusiform in shape, and obscurely fluctuating, but gave no crackling sound on palpation. There was no tenderness, the swelling was not inflamed, nor were the superficial veins dilated.

Operation was performed nine months after the onset of the condition. An incision directly over the swelling and slightly toward the palmar aspect revealed a thin shell of bone which on being removed exposed a cavity filled with 5 c.c. or more of thin, dark-brown liquid. The cavity extended upward, gradually diminishing in size until it ended halfway up to the elbow. It had a couple of ridges in it and laid near the surface. The cavity in its lower spherical part contained only brown liquid and no lining membrane. The upper conical portion was filled with a reddish granulation-looking material, soft in consistency, with no trace of any cartilage. This tissue was removed and the cavity thoroughly curetted and packed with gauze. Recovery was uneventful. At present, one year after the operation, the wound is firmly healed, there is no evidence of recurrence, and the functions of the part are perfectly normal.

Microscopic examination showed the growth to be a round-celled sarcoma with numerous giant cells.

Sarcoma is of interest both from the diagnostic standpoint and that of treatment.

Contrary to many reported cases this one gave no history of injury, though, owing to the youth of the patient such could easily have passed unnoticed. When first seen the general appearance of the enlargement, together with the age of the child and history of previous glandular trouble, caused it to be regarded as of a strumous or tuberculous nature. The skiagraph, however, of these cases shows the cystic character so distinctly that it should suggest the possibility at least of its being a cystic sarcoma, although, of course, the extreme rarity of a medullary cystic growth of the long

bones being present would cause one to hesitate in making such a diagnosis. The microscopic findings showed that

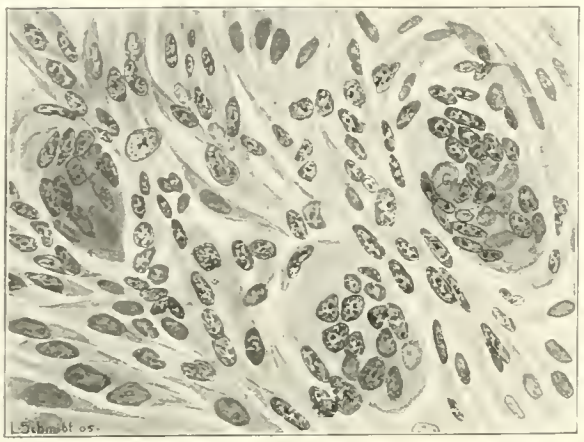

Fig. 2.—Section of the lining membrane of the cyst, showing sarcomatous tissue with giant cells.

the growth was a sarcoma composed of round cells and spindle cells in an almost homogeneous matrix with numerous giant cells (Fig. 2). It was evidently no simple benign cyst such as is said to originate from cartilage. That it was medullary was evident from its location; the bone had practically disappeared at one point, at the radial side, where the curette encountered the periosteum and soft tissues.

It has long been known that certain sarcomatous growths of the long bones, particularly when cystic and medullary in character and origin, and of the giant-cell type, are less prone to pursue a malignant course than those of the periosteal, solid and round spindle-cell types, and Dr. Bloodgood has recently drawn especial attention to the advisability of performing conservative operations in such cases. This seems to be one that supports his position. He claims that amputation is not necessarily indicated even when the muscle is infiltrated and that, as in the cases affecting the jaws, unnecessarily severe or even fatal operations for total removal are done when a simple curetting would have sufficed. If this growth were of the malignant type we would have probably already had evidences of metastases as the malignant type of sarcoma recurs after operative interference with great rapidity.

A COLLECTION AND AN ANALYSIS OF THE REPORTED CASES OF OSTEOARTHRITIS OF THE SPINE (SPONDYLITIS DEFORMANS).*

By Don Carlos Guffey, B.S., Ph.B.

Definition. Spondylitis deformans may be defined, in general terms, as a "disease characterized by alteration in the normal curves and restriction of the ordinary movements of the spinal column,"[1] but in more accurate and definite terms as a subacute or chronic progressive ankylosis of the vertebral column, characterized by structural changes in the bones, ligaments, and articular cartilages of the joints. It usually begins in the lumbar region and extends upward, and is nearly always associated with some deformity, usually dorsal kyphosis, and decrease in, or loss of, the normal lumbar lordosis. It may or may not be associated with involvement of the shoulder, hip, or other joints, and is not, as a rule, accompanied by spinal-root symptoms, such as paræsthesia, anæsthesia, etc.

Historical. The disease under discussion, though only recently brought prominently before the profession, is neither rare nor modern. It is true that not a large number of cases are reported, but this does not prove its rarity. There have been collected for this paper, with considerable difficulty, 131 cases. But, as a matter of fact, partial spinal ankylosis often exists without being recognized,[15] and it is not an uncommon thing to find a splendid specimen on the dissecting table.* There are at present two, and possibly three,† cases

* Awarded the Frederick A. Packard Prize in Clinical Medicine, University of Pennsylvania, 1905.

* A foot-note to Dr. Ogle's paper in vol. viii. of the Transactions of the Pathological Society of London reads: "Dr. Ogle remembered to have been told some years ago by the late Mr. Alexandre, the dealer in skeletons, that more or less complete bony union between the occiput and the first cervical vertebra had been found by him in one skeleton out of every 200 which he had to prepare for sale."

† Since writing this article one of these cases has left the hospital. The case is not included in the list to follow because it was diagnosed by the surgeon in attendance (Dr. Frazier) and the neurologist in consultation (Dr. Spiller) as a case of Pott's disease. It is hardly for me to say that it was a case of osteoarthritis, though such is my belief. The history follows:

Man, aged thirty-two years; Hungarian; miner. Father died of "dropsy;" rest of the family living and well; wife living; no children. No history of tuberculosis. Was a shoemaker for six years when in Hungary. Used alcohol to excess. Had blood poisoning in right arm. Furunculosis when sixteen. Jaundice nine years ago, but cleared up without treatment. Never had la grippe, rheumatism, or venereal disease. No cardiac symptoms. Present trouble began in 1902, when a rock fell on him, doubling him up with head between knees. Was not unconscious. Noticed lump in dorsolumbar region when released. Had severe pain, extending down thighs. Began regular work in three months. Had to quit work in a month because of pain and weakness. Pain made worse by jarring, flexion, and rotation. Spine became immobile in dorsolumbar

in the University Hospital, and two, at least, in the Philadelphia Hospital. That it is not modern is proven by the fact that a certain Egyptian mummy* 5600 years old (3700 B.C.) shows osteoarthritis of the spine.[25] (And who knows but that the bull-headedness and stiff back-bonedness of old Rameses II. was not due to this disease?) Nor can the human race claim it as its exclusive heritage, for the gorilla, the horse, the cat, and the ox suffer from it.[14] The statement is attributed to the great Aristotle (though probably incorrectly) that "all beasts have flexible necks except wolves and lions," and the explanation for the statement is that animals were seen which had osteoarthritis of the cervical vertebræ with ankylosis.[3]

NOMENCLATURE. This condition is but one of the many manifestations of arthritis deformans or osteoarthritis, and is rightly designated by Osler "the vertebral form of arthritis deformans." This term "arthritis deformans" should not be confused with the term "osteitis deformans,"[5] the former meaning deformity from disease of the joint, the latter from disease of the bone itself. The pathology of the two conditions is absolutely distinct.

Of the many terms used in connection with this trouble, probably the best of all is "osteoarthritis of the vertebral column," because the pathology is probably identical with that of osteoarthritis in other joints and the words "vertebral column" indicate the seat of trouble. Should a given case under consideration have the lesion in the hip or shoulder as well, we may designate the condition "osteoarthritis of the spine and of the shoulder or hip-joint." For this combination the French, through Marie,[6] have used the expression "rhizomelique spondylose," or, as we say, rhizomelic spondylosis. But really the term is of no use, is confusing and misleading, and should be dropped.

"Spondylitis deformans" is used by many writers, but it is easily confused with "spondylitis," which is the usual term for Pott's disease, or tuberculosis of the vertebral column. "Rheumatoid arthritis" is an older name for osteoarthritis, but the symptoms of the latter so little resemble rheumatism that the word "rheumatoid" is misleading and almost inaccurate. Likewise, "chronic rheumatic arthritis" is a bad term, since rheumatism probably has nothing to do with the disease except as a predisposing or causative factor. The clinical term "arthritis deformans" and the pathological one "osteoarthritis" are both good, but the latter is better, since it more nearly describes the actual condition present. "Rheumatic gout" is probably the worst name of all.

Since the condition is pre-eminently a chronic or progressive ankylosis, the Germans speak of it as "chronic or progressive ankylosing inflammation of the spine." "Rhizomelique spondylose" seems to be the favorite term in France. In England the term "spondylitis deformans" is largely used, though Sir Frederick Treves[7] refers to it as "chronic rheumatic arthritis of the spine." But it should be remembered that rheumatism never gives true ossification and that the pathology of rheumatism is never that of osteoarthritis. In this country various terms are employed: Osler[4] and Tyson,[8] "vertebral forms of arthritis deformans;" White,[9] "spondylitis deformans" or "osteoarthritis of the vertebræ;" Frazier,[10] "osteoarthritis of the spine;" Spiller,[11] "progressive ankylosis of the vertebral column;" Goldthwait,[15] "osteoarthritis of the spine or spondylitis deformans;" Strümpell,[16] "chronic ankylosing inflammation of the spinal column" (Baumler, Hoffa, Bregman, Hoffman); Kohler and Beneke,[2] "spondylitis deformans;" Oppenheim,[13] "arthritis deformans of the spine;" Beer,[2] "rigidity of spinal column;" Marie,[6] "spondylose rhizomelique;" von Bechterew,[12] "ankylosing inflammation of the spine;" Popoff,[2] "neuropathic curvature of the spinal column;" in England, "spondylitis deformans;" Ruhräh,[2] "osteoarthritis of spine or spondylitis deformans."

ABSTRACT OF CASES.

Ruhräh.[2] Female, aged twenty-two years. No hereditary history. Thrown from a horse at fourteen years, striking on right hip and shoulder. Had rheumatism at fifteen years. Pain began in injured hip and extended to other joints. Fall from wagon at nineteen years. Back soon became stiff; pain constant; menstruations irregular; back, neck, shoulders, and hips stiff; atrophy, chiefly about shoulders and neck; no tremor; trapezius contains nodules; other joints free. No improvement under massage, passive motion, hot baths, or, internally, arsenic.

Woman, aged twenty-five years;* dressmaker. No history; began over one year ago with sharp, stabbing pains in right of injury or tuberculosis. Worked with wet feet. Trouble

region. Since then has been taking all kinds of internal and external treatment (liniments, cupping, plaster jackets, etc.). Now has rigidity of spine in dorsolumbar region, with a low dorsal kyphosis and loss of the lumbar lordosis. Pain on jarring and on pressure over the lumbar spine. Bladder and rectal control normal. Has lost weight, and appetite is poor. Examination by Dr. Spiller shows weakness in the muscles of the legs, right particularly. Small area of anæsthesia on outer side of right thigh. Patellar and Achilles reflexes increased, particularly the latter. Tuberculin test (1–3–5 mgr.) negative.

* An abstract from Dr. May's article follows. The mummy was discovered by Petrie. The body was complete. Was at full length, in wrappings of linen, in a solid block coffin without a lid. It was in a tomb in middle of cemetery of Fifth Dynasty at Deshasheh. Fingers were crooked from disease. Man, aged fifty to sixty years. Skull normal, except maxillary joint. Here nodular outgrowths. Odontoid process elongated, with facet on anterior surface, where it articulated with a facet on the anterior margin of foramen magnum. Left maxillary condyle is twice its normal size, etc. Vertebræ affected in direct proportion to movability. No ankylosis.

* M. W. is in Ward B of the University Hospital.

ankle (sewing foot), only on motion. Skin was not red or hot. Then the left ankle and left knee became involved; later became stiff; later other joints became involved. At present there is also stiffness in the neck and shoulder, and great crepitus in temporomaxillary articulation. There is subluxation of the left knee. Tuberculin test negative. Patient thinks that massage, electricity, and baking have done the most good. The salicylates do not relieve the pain. A cast was applied, with bad results.

Fagge.[40] Quoted by Marsh.[24] Man, aged thirty-four years. One year ago spine became stiff. Rounded dorsal curve. Later right hip fixed. Died of chest trouble, following difficult respiration. Postmortem showed ankylosis of arches, spinous processes, and articular processes of vertebræ. The vertebræ were much softened. Ribs firmly and extensively ankylosed to vertebræ. Right hip ankylosed. There were tuberculous deposits in the mesenteric glands.

Le Branton.[27] Woman, aged sixty-seven years; overworked. Attack began with influenza six months ago. Then had severe, continuous pain in right shoulder. Moderate atrophy of, imperfect sensation, and tender points in right arm. This relieved. Four months later another attack. Sensation over upper arm disturbed. Dorsal kyphosis; slight scoliosis. Rigidity from first to tenth dorsal vertebra. Ribs fixed; breathing abdominal. Rest, jacket, stretching, cautery, salicylates, alkalies, KI, and tonics all failed. Some relief from hot baths. Left shoulder involved. Suddenly seized with obstinate vomiting, and died. Autopsy denied.

Ridlon.[28] Woman, aged twenty-five years. Although disease was greatly advanced she was so relieved by violent manipulations under anæsthesia that one-half the normal range of lumbar motion and chest expansion were regained.

Starr.[28] Man, aged forty-five years. Ribs ankylosed, yet he was able to play the clarinet—his occupation.

Goldthwait[15] (1899). Case 1. Woman, aged fifty-eight years; nurse; no rheumatism; history negative; caught in heavy rain; next day pain in neck and tenderness; pain increased rapidly. After four weeks sudden swelling on right side of neck, size of lemon; this remained. After five months patient improved, but neck remained stiff. Thickenings over transverse processses in neck; motion of left shoulder limited; muscles of left hand contracted; sensibility normal.

Case 2. Woman, aged seventy years. Ten years ago had fall on sacrum. Since then pain in back; dorsal and lumbar kyphosis; scoliosis; no paralysis; other joints free.

Case 3. Man, aged twenty-one years; steel-polisher. Gradual loss of power in arms and legs for one year. Spine rigid and flexed; other joints free; motion of left arm limited; patellar reflex exaggerated; muscular atrophy of both extremities.

Case 4. Man, aged twenty-nine years; laborer. Had two attacks of rheumatism some years ago. Two months ago had typhoid fever. Soon pain in back. Slight prominence of eighth to tenth dorsal spines. Limitation of motion in lumbar region. Wears leather jacket. Some bending forward and gradual ankylosis of lumbar and dorsal region. Ribs ankylosed and breathing abdominal.

Case 5. Man, aged twenty-four years. History negative; engineer; much exposed. Pain in back for five years. Complete ankylosis from pelvis to midcervical region. Ribs ankylosed, breathing abdominal. Other joints free. No signs of nerve pressure. Wears light spring-steel brace with much benefit.

Case 6. Man, aged twenty-five years. Fireman in gas-house. For last four months pain in feet, hands, and spine. Ankylosis from the pelvis to the midcervical region. Ribs ankylosed; breathing abdominal. Slight anterior bending.

Case 7. Man, aged thirty-two years; professor. Well until nervous prostration. Went abroad. Soon stiffness of neck and shoulders developed. Upper dorsal and cervical spine rigid; arms numb and weak; atrophy of muscles of shoulders, neck, and back; limitation in both shoulders; reflexes normal.

Case 8. Man, aged sixty-two years. In Civil War got rheumatism, and back has been stiff ever since. Neck painful for last eight months. Lumbar and dorsal spine ankylosed and free from pain. Neck is moved with great pain. Ribs move slightly on respiration. Sensation in right arm impaired. Thomas collar gave great relief.

Case 9. Man, aged thirty-four years; a currier. Five years ago had pain in shoulder, left knee, and right foot. Soon back became stiff. For three years acute pain in right heel. One year ago neck became affected; cannot breathe freely; ankylosis from pelvis to neck; straight; breathing nearly entirely abdominal.

Case 10. Woman, aged thirty-five years. Took cold; stiffness developed at once; this was three years ago. Great pain in neck ever since.

Goldthwait[15] (1902). Case 1. Man, aged forty-two years; seaman. A few months ago had shooting pains in chest and down legs; some limitation of spinal motion; breathing difficult because of pain. Relieved by plaster-of-Paris jacket.

Case 2. Man, aged thirty-eight years. Rheumatism for six to seven years. For last year has settled in right shoulder. Spine and left arm now painful. Loss in weight, thirty pounds. History negative as to rheumatism and tuberculosis. Complete spinal rigidity; hips free; right arm paralyzed and much atrophied; leather jacket and Thomas collar; kept in bed; tonics, forced diet, good general hygiene; lived out-of-doors. After six months, pain relieved and power in right arm returned. Wears light spring-steel brace. Now well, except that spine is stiff.

Case 3. Man, aged twenty-four years; hospital attendant. Three months ago sudden pain in back of left thigh. No injury, although was a football player. Spine flexed; scoliosis; spasm of spinal muscles; hips free; left psoas contracted. Relief by use of jacket, except for stiffness.

Case 4. Man, aged thirty-two years. History of rheumatism in family. Four years ago rheumatism for four weeks. For last four weeks has had severe pain in back, extending to neck, and worse after resting; spinal rigidity; muscular spasm. Jacket and spring-steel brace relieve him.

Case 5. Man, aged forty-five years; physician. Ten years ago, after exposure to draught, had attack of sciatica in left leg. Three years ago another attack, which lasted nine months. Present attack began nine months ago, with cramps in back. Body flexed and cannot be extended, except slightly after rotation, when something seems to slip. Hips free. Leather jacket, which had to be remoulded from time to time, gave great relief.

Lediard.[32] Man, aged fifty-eight years; miner. Began with pain in legs and right arm; stiffness in back and neck. Father had rheumatism. Now, fixation of head and neck absolute. Condition gradually gotten worse for last thirty years. Dorsal kyphosis; femora and tibia curved outward, formerly straight; chest fixed and flat; shoulders limited and crepitus; stooping posture; atrophy of muscles of pelvic and shoulder girdles.

Clutton.[31] Man, aged thirty years; cabinet-maker. Father had rheumatism. Patient had rheumatism at nine years. Right hip remained stiff. Six years ago had rheumatic gout. Three years ago pain and stiffness in neck. Getting worse. For three months left shoulder has been fixed. Whole spine is ankylosed; stands in stooping posture, with knees bent; large dorsal curve and right scoliosis; neck stiff; cannot turn head to right, but can to left; chest almost fixed; right hip and left shoulder limited.

Sturge.[30] Man, aged twenty-six years. Dealer in artificial flowers. Mother and brother had rheumatism; another brother had gout. Patient had gonorrhœa shortly before trouble began, eight years ago. Then had sudden onset of pain in small of back. Complains now of pain and stiffness in back; cannot stand up as he used to; back and neck getting stiff; chest does not expand; dorsal and lumbar kyphosis, large regular curve; neck fixed, chin poked forward; spine rigid, except in lumbar region; breathing abdominal; other joints free.

S. B. Woman, aged fifty-six years (looks sixty-five years). No other illness. History negative. Dorsal convexity, with left cervical scoliosis; no ankylosis (Sailer); pain on attempting to extend neck, which is flexed; hands show rheumatoid arthritis; right elbow will not extend; cannot elevate arms above the horizontal; muscles wasted; knees swollen and painful on motion, also ankles. Began in 1903 with pain and stiffness in muscles; crepitus in joints; all joints more or less involved; some ankylosis. (Ward B, University Hospital.)

McCarthy.[29] Case 1. Man, aged thirty-four years; weaver, formerly an acrobat. Father and uncle paralyzed. Had acute articular rheumatism when a child. Eight years ago fell down stairs, landing on feet. This caused pain in right hip. Disappeared. One year later pain reappeared in right hip and for last six years pain in both hips and lumbar spine. Dull ache, made worse by long hours of work. Had constant pain for two years, referred to pit of stomach. For two years nocturnal emissions and night-sweats; memory failing; typical flexed attitude at hips and knees; head fixed; rigid, awkward gait, with toes adducted, legs separated and flexed; rigidity of dorsal and lumbar spine; slight cervical flexion; other joints free; erector spinæ board-like and wasted; shoulder girdle wasted; reflexes of lower extremities diminished; sensation normal, except hyperæsthetic areas over trunk; nerve trunks not painful; pain on tapping over spine; chest expansion limited, breathing chiefly abdominal.

Case 2. Boy, aged eleven years. Began March, 1900, with swelling of feet and ankles, and pain and tenderness. In July hands were affected in same way. In April, 1901, wrists swollen, not very painful, fluctuation and grating in both. Fingers and joints of great toes involved. Now all joints of extremities are more or less ankylosed; spine involved throughout; slight motion in cervical region, but not complete ankylosis; symptoms of root involvement; wasting of shoulder girdle and extremities; hyperæsthetic zones on trunk; atrophy of skin about affected joints. Red blood corpuscles, 6,000,000; white blood corpuscles, 14,000; hæmoglobin, 60 per cent.

Case 3. Man, thirty-four years; fireman. All the joints were ankylosed, patient being rigid; entire spine was rigid and immovable. It was necessary to feed with liquid or semiliquid food.

Case 4. Man, thirty-five years. Song-and-dance artist. The disease began with an acute attack of pain and fever ten years previously; this was followed after a year's quiescence by a progressive involvement of all the joints, beginning in the right upper extremity and extending to all the joints in the body. The maxillary joints little affected. Spine rigid, with marked tenderness throughout entire extent; some movement present in cervical region. Marked kyphosis affecting dorsocervical area.

Case 5. Female, aged fifty-three years; housewife. Acute attack of pain and swelling began in the hands twenty-six years before, and extended to all the joints of the extremities, which later became ankylosed. Spine was almost rigid in the dorsal and lumbar areas, but quite movable in the cervical area; no curvature or tenderness.

Case 6. Female, aged forty-nine years; housewife. Disease began with an acute attack twenty-one years before, gradually affecting all four extremities, dorsal and cervical vertebræ; lumbar spine not affected; slight kyphosis in upper dorsal area; cervical area and all affected joints very tender.

Case 7. Male, aged thirty-one years; brickmaker. Acute attack began fourteen years before, with severe pain in lower extremities. Some time after this he fell and injured his spine and has not since been able to walk. Symptoms referable to the spine became much more marked after the injury. Disease progressed in the other joints until at the present time there is practically complete ankylosis of all the joints, including the jaw-joints. There is some kyphosis, with tenderness and pain referred to the cervical region; marked arterial sclerosis, with a systolic murmur over the apex of the heart.

Case 8. Man, aged thirty-three years; farmer. Acute attack occurred seventeen years previously, affecting ankles and knees; joints of lower extremities markedly involved, and to a lesser degree those of the upper extremities; jaws also; complete rigidity of the entire spine; considerable pain present, with tenderness; slight lateral curvature in cervicodorsal area.

Case 9. Female, aged sixty-eight years; housewife. Acute attack began thirty-two years before in right shoulder and wrist; since that time all the joints have become more or less involved; vertebræ were all involved, with some tenderness in the lumbar region and some slight lateral curvatures in the cervicodorsal; process most intense in cervical area.

Case 10. Male, aged thirty-six years; soap-worker. Acute attack began thirty-five years before, with involvement of the hands; history of injury in the hand, and arms first affected; main involvement found in upper extremity; some crepitus, with pain in the joints of the lower extremity, recent involvement of the cervical area of the spine; dorsal and lumbar areas completely ankylosed; an area of zonal anæsthesia corresponding to the scapula of the right side; some tenderness with slight kyphotic curvature in the cervicodorsal area.

Case 11. Woman, aged sixty-four years; housewife. Acute attack occurred twelve years before, after an attack of la grippe. Lower extremities first affected. This was followed by rigidity of the spine and later of the lower extremities. The affection of the spine was confined to the cervical and upper dorsal areas. The lumbar spine was little, if at all, affected. Some anæsthesia of trunk in middorsal distribution of right side.

Case 12. Man, aged sixty-three years; carpenter. Acute attack began fourteen years before, following la grippe. The ankles were first affected, later the joints of the lower extremity. Has had "lumbago" ever since the begining of the disease. Main involvement of spine was confined to the dorsolumbar area; there was considerable crepitus, with little limitation of movement in the cervical area. There was an area of anæsthesia of the trunk corresponding in distribution from the sixth to the tenth dorsal spinal segments, with a zone of hyperæsthesia above this area.

Case 13. Female, aged forty-nine years; housewife. Acute attack began twenty-one years before, after the birth of a stillborn baby. There was an acute painful swelling of the joints, with fever, affecting both upper and lower extremities. There was very marked atrophy of the muscles and also of the skin; marked deformity in all four extremities; spinal involvement confined to the cervical and upper dorsal areas, associated with distinct scoliosis and some kyphosis in the same area.

Case 14. Man, aged thirty-two years (apparently forty-five years). Electrician. Used right hand a great deal. Alcohol moderately. Father died of pleurisy. No injury; no other illness. Eight years ago had pain and stiffness in right wrist. Right fingers and left wrist soon involved; also ankles, feet, knees, hips, and spine. Examination: Lay in bed on back, semirecumbent, legs and thighs flexed. Emaciated; skin dry, glazed, and shiny; areas of brown pigmentation; œdema in feet; arteriosclerosis; muscular wasting; slight tremor; no contracture. Joints: right thumb and middle finger subluxated; little finger fixed, also right wrist; cannot raise arm above horizontal; neck very rigid; spinal movement limited; similar conditions in feet to that in hands; knees limited; right hip fixed; jaw limited; chest greatly limited in expansion. Reflexes increased; sensibility normal; hæmoglobin, 38 per cent.; red blood corpuscles, 5,130,000; white blood corpuscles, 21,200. Albumin and indican in urine.

Pathology. No gross changes in nervous system. Microscopic—Brain: arteriosclerosis; large cortical pyramidal cells of motor cortex show presenility (smaller in size, decreased number of dendrites, lessened quantity of chromatin, increased pigmentation). Cord: arteriosclerosis, with miliary aneurysms in pial vessels. Marchi method showed black granules, the result of sclerosis. Nerves: same sclerotic changes; not sufficient to constitute degeneration. Cervical and lumbar enlargements: ganglion cells of anterior horn diminished in number, increase of pigmentation, dendrites reduced in numbers, nuclei small and stained too deeply. Anterior and posterior roots: practically normal; some sclerosis. Spinal intervertebral ganglia: arteriosclerosis. The ganglion cells were seldom normal. Great increase of pigment; very small and eccentrically placed nuclei, which do not take the stain and are sometimes vacuolated. Gasserian ganglion is similar. Dr. McCarthy remarks that these changes in the sensory ganglia are of special importance in regard to the tropic changes.

Collins.[33] Man, aged forty-five years; soldier. Ten years ago gradually developed bending of the back and difficulty in moving one hip. In addition cessation of thoracic breathing and spinal rigidity.

Gibney.[33] Man, aged thirty-five years. Stooping for last five years. Gonorrhœa seventeen years ago. Four years later had seiatica in left leg, lasting about one year. In 1896 had much pain in heel, extending up into hip.

Sachs.[33] Case 1. Man. Began six years ago with pain in left knee. Chronic cough, but no tuberculosis. Under narcosis joints were rigid.

Case 2. Man, aged forty-eight years; Russian tailor. Began two and one-half years ago with pain in sacral and lumbar regions. No trauma; bent forward and to the left; spastic, paretic gait; knee-jerk increased and ankle clonus on both sides; tenderness of twelfth dorsal vertebra and below; later, lower extremity contracted; dragged left leg; suddenly pain increased and knee-jerk became absent; laminectomy; great improvement; dura was greatly thickened.

Case 3. Man, aged fifty-three years; Russian. History negative. Lower portion of spine and hip ankylosed.

Case 4. Man, aged fifty-four years. History negative. Had acute articular rheumatism. Present trouble began three years ago with pain in small of back. Thorough course of iodides caused great improvement. Walked stiffly. Diagnosis: pachymeningitis.

Collins.[33] Woman, aged thirty years. Had a fall; year later pain in back and soon great stiffness; bony tumor over sacrum; right shoulder stiff. Autopsy: Cord normal; spine one piece; anterior common ligament calcified, also posterior spinal and interspinal ligaments.

Peterson.[33] Man, aged forty years. Neurotic temperament. In three or four years he developed complete immobility of the spine and stiffness in hips and knees.

Gordon.[34] Case 1. Man, aged fifty-four years. Fifteen years ago fall from wagon, striking on head and neck. Intense pain and soon muscular wasting. Soon rigidity and limitation of motion in cervicodorsal spine and large joints. Has also symptoms of amyotrophic lateral sclerosis; involvement of sphincters.

Case 2. (Dercum.) Man, aged forty-three years. Injury to neck thirteen years ago; next day pain and stiffness in neck; this increased. In three years entire spine was rigid; hips also; several attacks of rheumatism; prominence of vertebræ from sacrum to head; neck flexed and ankylosed; scoliosis; large joints ankylosed; great, but irregular, muscular wasting; fibrillary tremor; reaction of degeneration; reflexes decreased.

Case 3. Woman, aged fifty-four years. One year ago attack of vertigo, with unconsciousness; unable to walk; sight and speech affected; several similar attacks after exertion; rigidity of spine without pain; other joints involved; ataxia in legs for five years, in arms one; arm-joints limited; frequent micturition, occasionally incontinence; over-straight; knees not flexed when walking; feet scrape floor; cannot raise arms much; head and neck rigid; face immobile and mask-like; all expression impossible; deglutition normal; jaw stiff; Argyll-Robertson pupil; gait ataxic and spastic; ataxia increased by volition; ankle clonus on right, also Babinski; reflexes exaggerated; reaction of degeneration; muscular atrophy of Aran-Duchenne type; sensation slightly decreased; girdle sensation; sharp, shooting pains in legs and arms; constant drawing sensation in legs; pronounced arteriosclerosis.*

Wood[35] (1856). Specimen from girl aged eighteen years. Ankylosis on both sides between atlas and skull and between axis and third cervical. All foramina for nerves and blood-vessels normal; inner side of canal smooth; spinous processes ankylosed, likewise transverse and articular processes; odontoid process more pyramidal than normal; lordosis of whole cervical spine; anterior roots of transverse processes of atlas absent. Dr. Wood thinks it was congenital.

Ogle.[36] Specimen. Occiput and atlas ankylosed; atlas and axis not ankylosed; other cervicals submitted were welded together in great flexion; how much of spine was ankylosed was not known; odontoid process greatly enlarged. History of case: Man, aged seventy-three years; tailor; insane; talipes varus of both feet; knees and hips contracted, but not ankylosed. Walked on his rump with his legs crossed tailor fashion. Some contracture of arms; had gout.

C. S., man, aged twenty-six years; driver; exposed to all kinds of weather; no rheumatism; began with pains in legs and back; stiffness of back and hips developed gradually; now complete ankylosis of spinal column and hip-joints; cannot raise arms above horizontal; bony outgrowths about shoulder; atrophy of muscles of shoulders and back; walks with crutches, pendulum gait. (This patient was in the Philadelphia Hospital, in the service of Dr. Mills, but is now at home.)

Von Borchard.[41] Man, aged thirty-eight years. Had trauma to head; intense pain on flexion. In half a year cervical spine became flexed with a dorsal kyphosis. Diagnosis: Kummell's fracture. In a few years the neck became greatly flexed and very painful. There is intense muscular atrophy. Diagnosis now: ankylosis of spinal column, Bechterew type.

Sachs.[20] Man, aged thirty-seven years; Russian tailor. History negative; at ten years had influenza; denies venereal disease; hard worker; began with pain in left knee six years ago; due to cold, he thinks; pain increased by movement; relieved by extension and was about again. Had chronic

* This case has been considered by some authorities to be one of amyotrophic lateral sclerosis.—Medical Record, 1904.

cough, but no tuberculosis; both knees became stiff; kept in bed ten months, resulting in rigidity of hips and lumbar spine. Examination: Emaciated; hips and knees rigid; scissor-leg gait; spine rigid; stooping posture, leaning to right; rests on a sloping surface; jaw free; nodding imperfect; muscles flabby; thorax flat; abdominal muscles rigid; electric reaction normal; right knee-jerk increased; increased myotatic irritability; atrophy of extensors of thighs and legs; knees fixed, no tenderness or redness; large dorsal curve in spine; no tenderness over spine. Under narcosis joints remain rigid.

Fraenkel.[20] Man, aged fifty-three years; painter. History negative; no exposures or severe cold; chancre thirty-two years ago; treated. Began eighteen years ago with sore throat. Had rheumatic pains all over, which settled in hips; no fever, swelling, or pain; progressive limitation of motion, extending to spine; head free; thorax normal; spine not tender to percussion or jarring; rigidity of lumbar region; muscles rigid; hips entirely ankylosed; other joints free; no muscular atrophy; sensibility and reflexes normal; gait is rotary; no exostoses.

Sachs.[20] Man, aged fifty-one years; depot master. History negative; lues thirty years ago. Years ago had inflammatory rheumatism. Present trouble began three years ago with pain in small of back; increased by movement; began to walk stiffly; became impossible to flex thighs or spine; right leg smaller than left from an old fracture; swelling of feet due to nephritis; knee-jerks increased; double ankle clonus; some dysuria and retention. Improved greatly under the iodides. Diagnosis: specific or rheumatic pachymeningitis.

McBride.[39] Case 1. Man, aged forty-eight years; soldier History negative. Began with pain in left big toe. Later left hip became stiff; this thirty years ago. Ten years later spine began to get stiff. Left arm at first paralyzed, then recovered, then got stiff. Later right arm and hip involved. Now entire spine stiff. Examination: Body and neck flexed; knees bent; hip-joints almost immovable; spinal muscles rigid, also muscles of arm; no pain, spasm, or tremor; hyperæsthesia on back; knee-jerks exaggerated; double ankle clonus; no muscular atrophy; scoliosis to left. Patient says spine was stiff before curvature developed. Spine somewhat tender; sits on his back

Case 2. Man, aged fifty-four years; laborer. History negative. One year ago fell, striking on forehead; unconscious; neck stiff and painful. Later arms got weak and muscles wasted. Pain in neck and arms. Examination: Neck and dorsal spine rigid; muscles of back, neck, and shoulders atrophied; also of arms; movements of hands limited; pain on pressure over fifth cervical. One year later showed progress of disease; breathing pectoral; incontinence of bladder and rectum. Diagnosis: hypertrophic cervical pachymeningitis.

Eshner.[39] Man, aged twenty-four years; laborer. Had rheumatism; cervicodorsal kyphosis, with rigidity of spine and large joints; general wasting; increased reflexes; sensibility normal.

Dercum.[39] Female, aged seventeen years. Had scarlet fever and mumps; irregular menstruation. Two years ago sudden pain in left knee. Walked lame for weeks; in bed for months with rheumatism; relieved. A year later pain in both groins; entire body wasted; thighs flexed; fixation in adduction; right knee limited; hyperæsthesia of abdomen, with rigidity; girdle sensation; pain on pressure over spine; knee-jerks decreased; lumbar and dorsal spine rigid.

Von de Buck and Debray.[42] Case 1. Man, aged thirty-two years. Arthritic family; sexual and alcoholic excesses; had typhus fever ten years ago; immediately following had girdle pain; paræsthesia of legs and pain in spinal column; some ankylosis of lower extremities. Now the body is bent forward with a dorsal kyphosis; knees slightly flexed; no ataxia; Kernig's sign; ankle clonus on right; left pupil larger; no atrophic disturbances. Bechterew type.

Case 2. Man, aged twenty-eight years. No arthritis in family. Had an accident years ago. Dislocation of left knee, which could not be replaced; then pain and ankylosis of right knee. Next year had a fracture of left femur; great pain in spinal column; muscular atrophy; patient was very nervous.

Von Glaser.[41] Presented case with ankylosis of articular processes of the vertebræ, associated with ossification of the ligaments (flava, apicum, interspinalia, radiatum). So-called supracartilaginous exostoses.

Pussep.[41] Man, aged thirty-six years. Mother had rheumatism and died suddenly. Twenty years ago noted pain and weakness in neck and a rigidity of the spinal column. Condition grew gradually worse; dorsal kyphosis; reflexes exaggerated; sensibility normal; muscular atrophy of neck, back, shoulders, and lumbar regions; abdominal respiration; diminished electric excitability; head flexed; sitting impossible; no syphilis; used alcohol moderately.

Von Chmelewski.[41] Case 1. Man, aged thirty-six years. Father died from heart trouble; mother hysterical. Patient is scrofulous and abuses venery. Had severe attack of gonorrhœa, followed by arthritis in hand and lower extremities; gait difficult; for three years pain in shoulder-joint, also hips and knees. Flexion of head difficult; spinal column entirely ankylosed; straight; muscular atrophy; abdominal breathing; scleroderma on chest and back; pruritus on face; partial degeneration of shoulder girdle; hypertonicity; rheumatoid pains in spine and large joints; electric reaction diminished; incipient pulmonary tuberculosis.

Case 2. Man, aged thirty-eight years. Syphilis, articular rheumatism, alcoholism. For about a year pain in right shoulder and cervical spine; ankylosis of spine, except in

cervical region; atrophy of muscles of back; abdominal breathing; pain on pressure over sternum, ribs, and spine; incipient tuberculosis.

Case 3. Woman, aged twenty-six years. Father had a nervous disease. Patient fell five metres; paralysis. For seven years difficulty in walking; ankylosis of thorax and limbs; atrophy of muscles; pain in back, shoulder, and hips; no degeneration.

Case 4. Man, aged twenty-five years. Father had nervous disease. One brother had rheumatism. Patient lived in damp places. Pain in sternum, right hip, right shoulder, and left hip. Amyotrophic symptoms in both hands; cervical kyphosis and ankylosis; neck free; abdominal breathing.

Case 5. Man, aged forty-eight years. Several colds; pain in right knee; cervical flexion limited; pain in head, neck, and back; lower dorsal kyphosis; total ankylosis; abdominal breathing; contracture of femoral adductors; hyperæsthesia of right leg; incipient tuberculosis.

Case 6. Woman, aged forty-eight years. Pain in hips; difficult walking; ankylosis; loss of patellar reflexes; femoral adductors and flexors contracted.

Winokurow[41] saw two cases at the begining of the disease, both during convalescence of typhoid. The first developed a spinal meningitis, which became chronic and was followed by stiffness of lower spine. He believes that a leptomeningitis s first.

Dana.[17] Man, aged thirty-five years; carpenter. No rheumatic history. Paraplegia from Caison's disease. Onset of this disease gradual, beginning with pain in knees and hip; constant and dull. Spasticity of muscles of thigh. Left knee first involved, then left hip, then right knee and hip; no swelling of joints and no crepitus; bladder and rectum free; thighs limited in extension, adduction, and rotation, probably due to spasm; no paralysis; compensatory lordosis; spinal rigidity in lower part. Condition partly disappeared under ether; reflexes exaggerated, both superficial and deep; no Babinski, but spurious clonus of right ankle; no anæsthesia or ataxia. Death sudden, from heart lesion. Postmortem showed no lesion of cord, except that lumbar enlargement was very small. Degenerative changes found in lining of hip-joint.

Osler.[18] Case 1. Male, aged thirty-three years. No injury and no hereditary history. Rheumatism for fourteen years in joints; pain in hips, not in back; rigidity of entire spine; dorsal kyphosis; atrophy of shoulder-girdle muscles; fixation of thorax; thickening of ankles and hand-joints; crepitus on motion; enlarged spleen; pigmented skin.

Case 2. Male, aged forty-two years. No injury and no hereditary history. Rheumatism in shoulder, hip, and wrists; gradual stiffness of spine; right knee enlarged; right shoulder limited in motion and tender; complete spinal rigidity, with moderate kyphosis; thorax fixed; little or no pain in spine; dorsal muscles hard and firm.

Case 3. Male, aged fifty-eight years. No injury and no hereditary history. Rheumatism four years ago; right knee and ankle swollen. Onset gradual, beginning in stiffness in back. Pain was great; numbness and tingling in legs; furunculosis; tremor in hands; voice changed; extreme spinal rigidity, with some kyphosis; marked atrophy of muscles of back, shoulders, and hand; movements of paralysis agitans; crepitus in joints of arms, but no swelling; extensive arthritis of right hip-joint, with shortening of leg; knees swollen; no osteophytes.

Case 4. Male, aged thirty years. No injury and no hereditary history. Rheumatism in one hip five years ago; progressive spinal rigidity; pain in back and side; now spine immobile; kyphosis; chest flat; pain in shoulders and back on movement; no sensory disturbances. Moderate wasting of muscles of trunk; hip and shoulders not affected; knee-jerk exaggerated.

Case 5. Female, aged seventy-two years. Gradual rigidity of spine, with great pain; extreme kyphosis; difficult deglutition; wasting of shoulder, back, and arm muscles; thorax fixed; great pain in back and sides.

Stockton.[19] *History of skeleton.* Man; stone-mason; died at forty-four years. Intemperate. Had gonorrhœal arthritis five years before. Absolute rigidity of all the joints; dark pigmentation of skin; marked atrophy, in legs especially. Grooves through which tendons pass unusually deep.

Sachs. Man, aged thirty-five years. Ankylosis of dorsal spine, with pain in and inability to move right arm. Pain radiated to right thorax. Atrophy of muscles innervated by dorsal segment.

Frazier.[10] Case 1. Man, aged forty-two years; freight agent. No hereditary history. Temperate. Chest crushed. Six months later complained of weakness in back and pain in hip-joints. Both hips and spinal column began to stiffen; head became bent forward; thighs and legs flexed; hips ankylosed; knees stiff; absolute rigidity of spine; dorsal and cervical kyphosis; atrophy of thigh particularly; tremor in leg muscles; no sensory disturbance; reflexes normal; spurious ankle clonus; bladder and rectum free; conditions unchanged under ether; chest flat and fixed; abdominal breathing.

Case 2. Man, aged twenty years; miner; temperate. Onset: sharp pain in right hip. One week later fell from car. Never been able to walk since; scissor-leg gait; hips ankylosed; rigidity of spine; atrophy; sensation undisturbed.

The following cases are translated from Schlesinger's article:[23]

Bechterew. Case 1. Woman, aged fifty-six years. Family history of spinal curvature. In last year developed a cervical and upper dorsal kyphosis. Feeling of heaviness in neck and a feeling as if it were welded together (Zusammengeschurt). Sometimes pain radiating to right hand. Spinal column limited in motion, but not tender. Slight wasting

of muscles on right side of neck, and some disordered sensibility in scapular region. Breathing abdominal; thorax fixed.

Case 2. Woman, aged fifty-two years. Mother and aunt had spinal curvature. Trauma twelve years ago. Since then pain in back and slowly developing kyphosis. Two years ago fell on back; since then rapid fixation. Marked curvature of cervical and thoracic portions. Head considerably fallen on chest. Normal lumbar lordosis lost. Lower portion of spine is completely immobile; no spontaneous pain; some by tapping on fourth dorsal vertebra; slight atrophy of shoulder-blade muscles; sensibility disturbed in distribution of first thoracic nerve; paræsthesia in hands and back; abdominal breathing; thorax fixed; in left foot ankylosis of two toes.

Case 3. Man, aged thirty-nine years. Repeated injuries to back, and has been in bent position for a long time. Mother was hump-backed. Cervical and dorsal kyphosis, with ankylosis; no pain; breathing abdominal; chest flat; paræsthesia in the legs; sensory disturbances about waist (girdle sensation).

Case 4. Mentally diseased without sufficient anamnesia. Has cervical and upper dorsal kyphosis, with complete ankylosis for ten years. Abdominal breathing without participation of the chest muscles. Reduced sensibility all over the body.

Case 5. Paralysis agitans; cervical and thoracic kyphosis; head sunken on chest and fixed; spinal column ankylosed and free from pain; disordered sensibility and paræsthesia in back, chest, and hand; atrophy of shoulder girdles; paresis of upper and lower extremities; contractures.

Case 6. Man, aged fifty-two years. Had syphilis. Fall six years ago. Two years later paræsthesia and pain in left chest, which later spread to waist. Paræsthesia in hands. Gradually developed kyphosis, cervical and dorsal, with ankylosis going from below upward. Spinal column not painful, except tender on strong percussion over third dorsal vertebra. Exaggerated tendon reflexes. Disordered sensibility of trunk; later, sharply limited hyperæsthetic zone at waist. Atrophy of shoulder girdle; later, pain in right shoulder-joint. Abdominal breathing; thorax absolutely fixed; intercostal spaces sunk in; slight weakness of the extremities.

Marie. Man, aged sixty years. Family history of curvature. A fall, followed by beginning curvature. Now an enormous kyphosis with ankylosis; slight scoliosis; no atrophy and no sensory disturbances.

Bechterew. Man, aged thirty years. Neuropathic mother, who was kyphotic. Syphilis two years ago. As official on railroad forced to make journeys. For four years pain in joints. General bending of body, especially in cervical region. On examination find high-grade kyphosis of cervical and dorsal portions; slight scoliosis to right, without compensatory lordosis. Head forward and fixed; spinal column ankylosed and somewhat painful on pressure; slight atrophy of shoulder girdle; slight sensory disturbance of upper half of chest and back; respiration abdominal; chest flat and fixed.

Schataloff. Case 1. Man, aged twenty-nine years. After catching cold eight years ago pain intermittent in coccygeal region (right) and for five years pain in side and back. Two years ago greatly exaggerated by lifting a heavy weight, and followed by progressive curvature. He has a marked kyphosis and cannot flex and extend dorsal spine; better in lumbar region; cervical not involved; tendon reflexes are diminished; sensibility normal.

Case 2. Man, aged forty-six years. Eight years ago trauma of spine. Since then pain in spine and weakness of legs; kyphosis of dorsal and upper part of lumbar region, with ankylosis; limitation of movement of neck; pain in lumbar region on bending; tremor of the hand; a little deafness; sensibility normal; patellar reflex diminished.

Schlesinger. Man, aged sixty-seven years. Thirty years ago trauma of spine. Patient was immediately bent forward and got worse. Had bad occipital neuralgia; kyphosis of upper dorsal spine; flexion greatly diminished; atrophy of shoulder-girdle muscles; sensibility normal; left hemiplegia; joints of hands and feet normal.

Strümpell. Man, aged thirty-nine years. History negative. Three years ago had pain in back and hip-joints; now ankylosis of spine, except in neck and upper dorsal portions; atrophy of corresonding muscles, which are fixed; contracture of muscles of right and left hips, worse on right; all other joints free; sensibility normal; skin reflexes normal; patellar reflex diminished.

Marie. Case 1. Man, aged thirty-one years. No heredity. About twenty years ago had marked pain in wrist, without swelling. Afterward swelling of both knee-joints and pain in left hip-joint. Ankylosis of right hip and a year later ankylosis of spine and left hip. The spinal ankylosis began below and ascended. One year later limitation of muscles of shoulder-joints; later, other joints involved; now spinal column is perfectly ankylosed, except slight motion in neck; normal lumbar lordosis is gone; marked right scoliosis in cervicodorsal region; hip-joint fixed in moderate flexion; shoulder and knee-joints limited in motion; exostoses on sacrum and on posterior pharyngeal wall; thorax fixed and breathing abdominally; no marked muscular atrophy or sensory disturbances.

Case 2. Man, aged forty-one years. Used to do hard work with shoulders. Years ago had great pain in knee-joints; afterward severe trauma from fall, which was followed by marked neuroses. From that time marked loss of flexion of spinal column. Intense pain all along the spinal column; afterward some pain in hip-joint and slight ankylosis. Ex-

amination reveals fixation of spine in lumbar region, not so marked above. Hips absolutely ankylosed; flexion of knee diminished; exostoses on second left metacarpophalangeal articulation; shoulder girdle slightly atrophied; fibrillary tremor of muscles in one part; sensibility normal; muscles of spinal column fixed; abdominal breathing; exostoses in pharynx.

Case 3. Man, aged twenty-eight years. Two years ago took heavy cold. After some years had a torticollis; some loss of motion in right hip and right shoulder; spine fixed in flexion; elbows, hands, and knees have crepitus; some pain all over body.

Braumler. Man, aged twenty-five years. Had disease seventeen years ago, after which developed ankylosis of both hip-joints. Occupation, book-keeper. Lumbar spine ankylosed. Great pain in neck and difficult flexion of neck, with fixation of head. Left sternoclavicular articulation painful and swollen.

Mutterer. Man, aged fifty-eight years. No history. Eight years ago had pain in back. Four years ago had marked ankylosis of spine. Caught heavy cold before ankylosis. Spine is completely ankylosed, with cervicodorsal kyphosis; lower part is in extension; rest of body free; the long back muscles are atrophied; both hip-joints are ankylosed in flexion; shoulder limited in movement; both knees are swollen and cannot be fully extended; muscles of shoulder girdle not atrophied, while those of the lower limb are slightly atrophied.

Schataloff. Man, aged fifty years. Nineteen years ago had pain in lower extremity and lower spine only on flexion. Nine years ago loss of flexion of spine. Five years ago loss of flexion in neck. Great pain on flexion of hip; kyphosis in cervical and upper dorsal region; lower portion of spine in full extension and fixed; flexion of hips diminished; crepitation in knee; atrophy of left upper and lower limbs; diminution of electric excitability; tactile and thermal sensation diminished on external part of right lower extremity; hyperalgesia of left lower extremity; patellar reflex diminished; skin reflexes diminished.

Spillmann and Etienne. Man, aged fifty-three years. Worked hard with shoulders. Some years ago noticed loss of power in legs and immediately a loss of motion in hip-joint. No pain; no paræsthesia; no joint swelling; hips absolutely ankylosed; ankylosed kyphosis; no disturbance of nervous system.

Beer. Man, aged forty years. Pain for some years in lumbar spine. Total loss of flexion, which began below; lumbar lordosis lost; thorax fixed; abdominal breathing; hyperæsthesia of muscles of back; hip-joints in flexion.

Saenger. Man, aged thirty-five years. Complete spinal ankylosis; cervical kyphosis; hips free; left hip-joint a little abnormal; thorax fixed; breathing abdominal; hyperæsthesia of thoracic muscles; atrophy of pectoral and back muscles; on loss of electric contractility.

Hoffmann. Man, aged thirty years. Began some years ago with pain in lumbar region. Since then has had pain in spine; pain on movement in both shoulders; acne on back; normal lumbar lordosis lost; flexion slightly limited; no pain on pressure over spine; other joints of lower extremity not much involved; atrophy of left deltoid and left upper arm; pain on pressure over brachial plexus; patellar reflex diminished; sensibility normal.

Bechterew. Case 1. Man, aged thirty-four years. Family history negative. When a soldier at twenty-one years had swelling of one knee-joint. At thirty-two years had a swelling of left shoulder-joint which extended up neck and down arm. Cause, he says, was a heavy cold; loss of power in hand and pain on flexion; ankylosis of entire spine; hips ankylosed in flexion; atrophy of muscles of neck, with fibrillary tremors; eye reflexes diminished; swelling of foot, hip, and knee.

Case 2. Man, aged twenty-seven years. History negative. Fifteen years ago had intermittent pain in knee. One year later had hydrarthrosis. At seventeen years cramps in muscles, followed by atrophy of muscles of upper left and lower limbs. Afterward right limbs became affected; then ankylosis of lower spine and hip-joints; no fever. Examination: Atrophy of right limbs and shortness of 1.5 cm. of right thigh; knee-joints limited; ankylosis of entire spine; no pain on pressure and no exostoses; sensibility normal; electric reaction normal; loss of patellar reflex.

F. Schultze. Woman, aged thirty-nine years. Brother had a pseudomuscular hypertrophy and an atrophy of the muscles of the small joints. He died of this. Patient well until twenty-seven years old, when she noticed stiffness in back and some pain in gluteal area. Stiffness became greater; later, knee-joints thickened and ankylosed; cervical ankylosis and hence head fixed; ankylosis and pain in shoulder-joint. Examination 1894: Ankylosis of hip and spinal column is complete; head fixed and turned to right; sternomastoid muscle in a tonic spasm; knee-joints thick and have little movement; shoulder and jaw ankylosed; deltoid atrophied; no nervous symptoms. In 1898 the disease was more pronounced; head absolutely fixed; also hip and knee; mouth can be opened a very little; no pseudohypertrophy; patellar reflex exaggerated; reflexes of upper extremities are diminished; normal sensibility; marked atrophy of muscles of small joints.

Jacobi and Wiardi. Case 1. Man, aged twenty-seven years. When very young noticed stiffness on flexion. At twenty-three years ankylosis of shoulder-joint, without swelling or fever. One-half year later jaw limited; mastication painful. Two years later knee became stiff, and six months after this left shoulder. Later stiffness of the back and limi-

tation of head movement; no pain; elbow and hand became stiff, but fingers free; a kyphosis at second dorsal vertebræ; ankylosis of lumbar region in extension; a scoliosis to the left in the cervical region; tendon reflexes exaggerated; abdominal and plantar normal; no paræsthesia.

Case 2. Woman, aged sixty-four years. Six years ago noticed stiffness of knee. Now stiffness of hips, shoulders, elbows, fingers, and jaw. Spinal column completely stiff. Angular kyphosis at dorsal vertebræ, with slight scoliosis to right; thorax fixed; sensibility normal; no reactions of degeneration.

Popoff. Man, aged twenty-three years. After a heavy cold had pain in back and knee. This improved, but came again in spinal column. After three months the spine became fixed in flexion. Two months later swelling and redness of right thumb. Wrist has been ankylosed for six years, with very great pain. Ankylosis of spine, except in cervical region; pain in back, but not marked; abdominal breathing; no atrophy; sensation normal; reflexes normal.

Garne. History of woman in whom there was fixation of spine and hips. Costal and neck joints not involved; no crepitus; no exostoses. It is remarkable that she had, three years ago, a disease exactly like this, but got well.

Hoffa. Woman, aged twenty-eight years. No heredity; never ill. At thirteen years noticed heaviness in legs; at twenty-five years she got an acute disease, marked by pain in limbs and exanthema. After that appeared a stiffness of the joints and of the back. One year ago had intercostal neuralgic pains on right side. Not complete stiffness of back and hips. Paræsthesia of arms and legs. Examination: Ankylosis of lumbar spine, upper spine being free. Movement of hips limited; crepitus in right shoulder; dorsal flexion of foot limited; other joints normal. Muscles of back are very firm, but are not stiff under ether. Even hip is more flexible under ether, but the spine is not.

Mery demonstrated a man, aged thirty-eight years, with ankylosis of spine and hips; shoulders slightly involved; pain in shoulders, none in back.

Leri. Case 1. Man, aged thirty-nine years. Had gonorrhœa. After a heavy cold had acute rheumatism of joints, associated with peliosis rheumatica; immobility of spine, afterward stiffness of hip and knee; head bent forward; a marked kyphosis; spine painful; cervical ankylosis; normal lordosis lost; hip and knee ankylosed; jaw, shoulder, and foot partially; all movements painful; legs are œdematous; thorax flat; abdominal respiration; no nervous symptoms.

Case 2. Man, aged thirty-five years. Mother had rheumatism. In 1881 had gonorrhœa. In 1886 pain began in lumbar region. Three months afterward a re-attack with disease of joint of right thumb; no fever. After eight years great pain in joints, with ankylosis of jaw; spine not movable; no pain; head fixed; dorsal kyphosis; no lumbar lordosis; pain on flexion and palpation; right hip limited; left not so much; hands and fingers of right side very painful; crepitus in shoulder-joints; atrophy of muscles of back; slight hyperæsthesia.

Valentini. Case 1. Man, aged thirty years. At twenty-four years had trauma. After that great pain in back, which was the same for years. After two years pain in right hip, and soon in left hip. Head, neck, dorsal and lumbar ankylosis; slight scoliosis; right sternoclavicular articulation is thick; crepitation; left shoulder is limited; hip ankylosed in flexion; knee in flexion also; others normal; nervous system normal.

Case 2. Man, aged thirty-two years. Had rheumatism; now stiffness of spine, hip, shoulder, and jaw.

Bregmann. Man, aged thirty-eight years. No traumatic or specific history. Shoemaker for years. Has noticed for some years a bending of his back, associated with pain and paræsthesia in upper and lower extremities. Great dorsal and cervical kyphosis; lumbar portion extended and stiff. The head only has some movement; patellar reflexes diminished; sensibility disturbed.

Feindel and Froussard. Man. After military exercise had pain in joints of left lower extremity, followed by ankylosis of spinal column, associated with pain in the back and lumbar region. Spinal column is kyphotic and ankylosed. Left hip-joint stiff and movements of shoulders diminished; crepitus; Bouchard's nodosities; thorax flat; breathing abdominal; atrophy of muscles of neck, pectoralis, trapezius, rhomboidei, and sacrolumbales; fibrillary tremors; marked knee-jerk; skin reflexes weak or lost.

Milian presents two patients. Head very much flexed forward; thorax flat, and its muscles very much atrophied. In one patient the bones are hypertrophied, except those of head, hands, and big toes; joints are free; epiphyses hypertrophied, and therefore some difficulty in movement. A very intense anæmia.

Heilizenthal. Case 1. Man, aged twenty-nine years. No specific history. Two and one-half years ago he developed a flexion of and a difficulty in movement of thorax. Soon there occurred pain in his legs and swelling of the joints. In a few months developed swelling of the joints of right upper extremity. Spinal column involved, but painless. Lumbar lordosis lost. Movements are possible in the neck region only. Movement of right shoulder limited. Crepitus great on flexion and associated with pain. Both knee-jerks are very much diminished; clonus of foot; no muscular degeneration; sensibility normal.

Case 2. Man, aged fifty-nine years. No family history. At twenty-four years had gonorrhœa and syphilis. Four years ago had a heavy cold and developed a difficulty in movements of the neck; then pain, swelling, and ankylosis of both knee-joints; crepitus. Pain in right hip-joint,

shoulder, elbow, hands, and fingers. The entire spinal column, including head, is entirely ankylosed. Neck and thorax fixed in extension; slight movement in lumbar area; nothing on palpation; hip-joint fixed in adduction; knee-joints fixed in flexion and thick; shoulder and elbow much affected. Right wrist is deformed and ankylosed, also the joints of the fingers and metacarpophalangeal joints. The ankles and toe-joints are ankylosed and painful. Jaw is movable, but painful. Sensibility normal.

Case 3. Man, aged thirty-nine years. Two years ago had monoarticular rheumatism of right knee-joint. During convalescence developed pain and stiffness in back, extending to left leg. Examination: Ankylosis of lumbar vertebræ and lower and middle dorsal; dorsal kyphosis; normal lumbar lordosis lost; nothing on palpation; muscles near spinal column are rigid; crepitus in right elbow; great atrophy of muscles of lower limbs; fibrillary tremors; patellar reflexes diminished; sensibility normal in thorax; slightly lost for quality in left lower limb.

Case 4. Man, aged fifty-four years. Always well before. For one year noticed a difficulty in movement of the spinal column. In one night there developed a marked stiffness of the neck and head; no pain in spinal column; swelling and thickness throughout length of spinal column. This afterward disappeared. No syphilis or gonorrhœa. After an intense cold had pain in knee and elbow, associated with stiffness. Examination: Head much flexed; cervical and dorsal ankylosis; slight lumbar movements; shoulder and hip-joints free; elbow and knee-joint affected; sensibility normal.

Case 5. Woman, aged sixty-four years. Icterus in family. Has had attacks of jaundice. For some years has had a stiffness in the spinal column, which developed from below upward. After six months the neck and upper part of the spine involved. Examination: Entire spine ankylosed, with head bent forward; great cervical and dorsal kyphosis; œdema throughout length of spine; elbow-joints free; hand and finger-joints involved, the skin being intense red, and active and passive motions very limited; hip-joint painful on active motion; knee-joints painful and thick, also ankle and toes; difficult deglutition; slight atrophy of shoulder muscle; atrophy of interosseous muscle; disseminated hyperalgesic zones.

Schlesinger. Man, aged forty-nine years. Fifteen years ago had intense pain in lumbar region. Eight years ago developed stiffness of neck and spine; pain in shoulders, hips, elbows, knees, and finger-joints. For three months the pains have been intense; pain on mastication; alteration of speech. Examination: Cervical kyphosis and head fixed; thorax fixed, abdominal breathing; slight atrophy of shoulder girdle; crepitus in large joints.

Beer. Man, aged forty-seven years. Had gonorrhœa many times. For three years pain in lumbar region and back; flexion of neck; thorax fixed; rigidity of muscles of back.

Marie. Man, aged thirty-one years. Had gonorrhœa many times. Gonorrhœal arthritis in ankle. One year later pain in cervical vertebræ. Head turned to right and not movable. Entire spinal column fixed, with ankylosis of hip and knee-joints.

Raymond. Man, aged twenty-six years. After attack of gonorrhœa had pain and stiffness of spinal column and hip-joints.

Rendu. Reported a case in which occurred, three years after an attack of gonorrhœa, an ankylosis of the upper part of spinal column, associated with arthritis sicca of shoulder-joints.

Renauld. Man, aged forty-three years. Had gonorrhœa three times in five years. Now pain in lumbar spine, shoulder, and knee-joints. Stiffness in shoulder-joints. Six years later had gonorrhœa again, and after fourteen days of the attack had intense pain when using the joints. Examination: Kyphosis and scoliosis; spinal column ankylosed; contractures of fingers of right hand and toes; nodosities on vertebræ; hip-joint limited in abduction; also limitation in arm; crepitus; thermoanæsthesia in arm.

ANALYSIS OF CASES REGARDING ETIOLOGY.

What the underlying fundamental causative condition is we do not know. Whether it is a trophic neurosis, a disturbance in metabolism, an infection, or a toxic condition, we cannot say. Whether trauma, exposure to cold and wet, infection, as gonorrhœa, or rheumatic disorders are predisposing or exciting causes it is impossible to affirm with absolute certainty. The last-named factors we may discuss more fully.

It is to be noted, in the first place, that about 75 per cent. of the cases occur in men. Of the total number collected 18 per cent. were reported at twenty to thirty years of age, 35 per cent. at thirty to forty years, 16 per cent. at forty to fifty years, and 24 per cent. after fifty years. Remembering that many of the cases had their disease for years before being reported, we can state with certainty that most cases occur between the ages of twenty-five and forty-five years (50 per cent. of the above cases). Osler[18] reports a case at seventy-two years, a woman, whose history is given above. Ogle[36] deseribes a specimen from a man of seventy-three years. Sunol[37] reports a case as young as thirteen years. Eulenberg, quoted by Sturge,[30] reports a child of twelve years; McCarthy,[29] a boy of eleven years. This seems to be the youngest case on record.

The most constant antecedent factor seems to be exposure to cold and wet. In 36 out of the 131 cases here collected this seems to have played an important role (27 per cent.).

Probably the next most constant factor is traumatism. In 23 out of the same 131 cases we have such a history (18 per cent.). The fact that of the 131 cases 98 are in men (75 per cent.), and at that age, middle adult life, when exposure to injury and to inclement weather is most frequent, points strongly to these as causative factors. Likewise the disease occurs in those whose occupation requires such exposure or great strain to certain joints. Thus, in hod-carriers the shoulder often becomes affected first, then the spine. In these 131 cases 21 show exactly such a history (16 per cent.). This theory of exposure is borne out by the fact that it occurs in horses, cats, oxen, and gorillas. A study[9] of sixteen skeletons of gorillas in European museums shows osteoarthritis in five. The argument may be made that since the Egyptian mummy had osteoarthritis and lived in a climate ideal for the treatment of such a condition, exposure could have nothing to do in the causation. That the mummy was a visiting stranger is improbable. But it is to be remembered that the Egyptians wore clothes which exposed them to every change in atmospheric conditions.[25] The fact that large joints suffer most from trauma and exposure, and that it is these joints which are chiefly involved in osteoarthritis, which is most frequent in men who are subject to these conditions, seems to lend weight to the probability of its relation to exposure and trauma. Moreover, it is more frequent in those who live in the country and whose exposure is undoubtedly greater.

Heredity probably plays some role in causation. We find such a history in 10 cases. The first case reported by Dr. McCarthy combines all of these possibilities—viz., age, trauma, exposure to cold and wet, gonorrhœa, rheumatism, occupation.

It seems, moreover, to be a disease of the poor; at any rate, of those poorly nourished, whose hygiene is bad, and whose life is burdened with care.

There are those who claim for it a neuropathic origin. Among the reasons for such a belief are mentioned the etiology, the muscular atrophy, the contractures, and occasional skin dystrophies (as pigmentation, local sweating, etc.). The relation of cause to effect, or which is the cause and which is the effect, is not clear. As to the muscular atrophy, contractures, and skin dystrophies, these seem to be the effects rather than the cause of disease. Some claim has been made that tachycardia, bronzed and discolored spots on the skin, clamminess of the skin, and pain in the muscles of the forearm are premonitory signs of osteoarthritis. If this is so, which it is to be hoped is so, for the sake of treatment, the neuropathic origin seems very probable.

Among other assignable causes are certain of the infectious diseases—viz., gonorrhœa, influenza, tuberculosis, and rheumatism. In 13 cases there is a history of specific urethritis, and in 22 of rheumatism. As to rheumatism, however, it may have been that the preceding attacks were those of arthritis deformans, and not true rheumatism.

Analysis of Cases Regarding Symptomatology.

The onset is generally gradual and insidious, beginning usually with pain and stiffness, which may be regarded as the earliest symptoms. But the onset may be very acute and severe.

Pain. The pain may be felt in the small of the back, interfering with stooping; or in the neck, interfering with nodding and rotation. It may be severe or mild, sharp or dull, at the site of the lesion or referred, constant or paroxysmal, unilateral or bilateral. Like the limp of tuberculous joint disease it is worse after rest and gets better by movement. Unlike neuritis the pain is felt in the nerve endings and not in the course of the nerve trunks. Pain is usually elicited by pressure, but may be spontaneous as well. It usually gets less severe as the disease advances, probably due to contraction of the tissue relieving the pressure on the nerve roots. There may be hyperæsthesia, paræsthesia, and anæsthesia. These are probably the result of pressure by bony outgrowths against the nerves in the intervertebral foramina. This accounts for the neuralgic type of pain. Pain may be elicited by jarring the head or heel, but not so marked as in Pott's disease.

Limitation of motion is usually greater on one side than on the other, and is usually first noticed in the arm when an attempt is made to raise it above the head, or in the chest on deep inspiration.

Later Symptoms. 1. *Spinal Rigidity.* The limitation of motion gradually increases, showing first in the lumbar region, as a rule, and then travelling slowly upward. In time the whole vertebral column may become stiff, as if the vertebræ were soldered together. This may be partial or complete, and when partial is usually confined to the lumbar region, occasionally to the cervical. The articulations between the skull and the atlas, and between the atlas and axis may become involved, so that nodding and rotation of the head are impossible. The odontoid process itself may become enlarged. This occurred in the mummy described by May.[25]

To account for this spinal rigidity we have to revert to the pathological findings: (*a*) a locking and coalescence of osteophytes from adjacent vertebræ; (*b*) bony union of the bodies of the vertebræ themselves; (*c*) conversion of the ligaments into bone, usually the anterior common ligaments; (*d*) the spines and laminæ may be united; and (*e*) the costovertebral articulation may undergo ossification. Muscular spasm from irritation is an important cause of rigidity, and it is to this probably that that rigidity is due which is relieved by

treatment, for it is not tenable that treatment can reduce bony changes.

2. *Spinal Deformity.* The most common is a dorsal kyphosis (a dorsal convexity). Along with the dorsal kyphosis, and partially as its cause, there is a loss of the normal lumbar lordosis. This is partially explained by the fact that in the lumbar region the intervertebral disks are thicker anteriorly than posteriorly (causing the normal anterior convexity in this region), and when they are destroyed the anterior surfaces of the vertebræ are brought together and the lumbar column is straightened. That these dorsal curves should occur at all is made plain when it is remembered that posteriorly the vertebræ rest against each other through their laminæ and transverse processes, while anteriorly they are separated by the intervertebral disks, which, when absorbed, allow the bodies to fall together. Muscular atrophy and loss of muscular tone may facilitate deformation, but they do not seem to be the chief causal factors. On the other hand, muscular spasm is a factor in the causation of deformity.

As a result of this the patient stands in a stooping posture, and the actual, as well as the apparent, height is diminished. He sinks upon himself, or, as Thebault[26] has graphically and humorously put it, "he looks at his umbilicus."

Should the changes be unilateral a scoliosis will result, with its convexity toward the sound side.

3. His *gait,* even when the hips are not involved, is peculiar, a sort of shambling gait, irregular and difficult. He stands with his knees bent and his toes turned out. His position on lying down is still more striking. In complete ankylosis it is impossible for his shoulders and hips to touch the bed at the same time—the rocking-chair condition. The usual sleeping posture is on the side or propped up in bed. When ankylosis of the thighs takes place in adduction we have a scissor-leg gait. Dr. Frazier[10] reports one case of scissor-leg gait, and another in which the position, patient lying down, was that of a Z.

Rarely the patient sits over-straight, as if he had swallowed a ramrod (poker-back). We have an explanation for this in the fact that such cases develop rapidly, so rapidly that ossification takes place before atrophy of the intervertebral disks can occur. The histories include 8 cases.

4. The *chest* and *pelvis* are often *flat;* the former from changes in the bony thorax, the latter from atrophy of the muscles. The chest is, in addition, often fixed, so that expansion is impossible, necessitating abdominal breathing. The fixation is the result of ankylosis of the costovertebral articulations, especially those between the ribs and the transverse processes. Ossification of the ligaments and ankylosis of the vertebræ may add to this. Thoracic fixation was found in 38 of the cases. This condition influences largely the prognosis.

5. *Exostoses* are frequently found. They are usually located along the anterolateral aspect of the vertebræ, but may be anywhere. By interlocking with each other they constitute one cause of the spinal stiffness. They may interfere with deglutition when in the cervical region. This is reported in 3 cases. It is probable that the nervous symptoms are the result of pressure by exostoses on the nerve roots. Likewise the changes found in the cord and spinal meninges are the result of pressure.

6. *Ankylosis of other joints* may occur at any time and in any order. The most frequent are the hips and shoulders, but any joint in the body may be involved, even the temporomaxillary articulation.

7. *Atrophy* of the muscles occurs, especially of those concerned in movements of the joints affected, and, therefore, chiefly the muscles of the back, shoulder, and hip. The atrophy is probably the result in part of disuse; in part of pressure on the trophomotor fibres.

Types. According to Osler[18] there are three types of the disease—viz.:

1. Children with large spleen and lymphatic glands (Still).

2. Atrophy of joint structures and ligamentous thickening without osteophytes.

3. Nodosities, ring-bone, and exostoses.

It is hardly necessary to separate the second and third classes, but better to consider them as the atrophic and the hypertrophic forms of the adult type.

The juvenile form, or Still's disease, occurs usually before the second dentition. It is characterized by elastic, fusiform enlargements of the joints, without bony change, but associated with lymphatic and splenic enlargement. Stiffness develops, the result of proliferation of the soft parts. Limitation of motion and muscular wasting may be great. There is no crepitus. "The onset is sometimes acute, with fever and even chills."[21] Any of the joints may be involved, even the spine, thereby becoming one of the forms of osteoarthritis of the spine. There is no tenderness or pain except on motion. The glands involved are those in association with the joints. They are hard, separate, not tender, and show no tendency to break down. The blood shows a secondary anæmia. There is a hyperplasia of the lymphatic glands and of the lymphatic tissue of the Malpighian corpuscles. Morse believes it to be an infectious arthritis.[22]

It has been usual to speak of the von Bechterew and Marie-Strümpell types of spondylitis deformans. The von Bechterew type is characterized by the following points:

1. Rigidity of the spine, with fixation of the thorax.

2. Kyphosis, chiefly upper dorsal spine.

3. Weakness, with atrophy of muscles of neck, back, and extremities.

4. Disturbance of sensation—paræsthesia, pain, etc.

5. Spine only involved.

The Marie-Strümpell (rhizomelique spondylose) varies thus:

1. Rigidity of spine, occasionally fixation of chest.
2. Involvement of hips, shoulders, and possibly other joints.
3. Nervous symptoms much less pronounced.

Now it does seem (true, a very bold statement) that this matter may be wonderfully simplified without the sacrifice of a single truth, considering them modifications of each other; thus:

1. Rigidity of spine, with more or less thoracic fixation.
2. Deformity, chiefly dorsal kyphosis.
3. Weakness, with more or less muscular atrophy.
4. Possible involvement of hips, shoulders, etc.
5. May or may not be nervous phenomena.

Pathology. The pathology is, so far as we know, that of osteoarthritis elsewhere. It involves the bones, articular cartilages, and ligaments.

The disease probably begins in the ligaments and periphery of the articular cartilages as a proliferation of the cells of the deeper layer. The centres and areas of pressure undergo atrophy. The interstitial tissue is the last to give way, which in so doing allows the free ends of the vertebræ to come into apposition. As a result, fusion of the bodies of the vertebræ occurs. Ruhräh says there is no atrophy of the bones.[2] The ligaments undergo change, resulting finally in ossification. The process usually begins on one side anteriorly and extends up and down the anterior lateral ligament. It may remain limited, or it may extend to the whole spine. The hypertrophy of the cartilage, with subsequent ossification, often gives rise to osteophytes or exostoses, and it is probably the pressure of these nodes on the nerve roots or cord that gives rise to motor and sensory symptoms.

Autopsies which have been reported show "ankylosis of the vertebræ, ossification of the ligaments, proliferation of the osseous tissue in the periarticular structures, and the presence of exostoses."[10] In Dana's case[17] a postmortem showed no lesion of the cord, except that the lumbar enlargement was very small.

The autopsy[38] in one of von Bechterew's cases showed the bodies of the vertebræ in the upper thoracic region to be in contact anteriorly. There was degeneration of the roots, especially the posterior, in the lower cervical and upper dorsal regions. The posterior and anterior columns presented degeneration. The pia was thickened on the posterior part of the cord in the upper thoracic region. There was degeneration of the spinal ganglia.

The pathological examination made by Dr. McCarthy[29] in the case reported above does not seem to show any conditions which are not explained by the arteriosclerosis present in that case.

It would seem, in the light of our present knowledge, that the changes which have been found in the spinal cord and its membranes are the result rather than the cause of the changes found in the osseous system.

Diagnosis. 1. Pott's disease, or spondylitis, is really the only condition with which spondylitis deformans should be confused. The symptoms common to both are spinal deformity, pain, loss of weight, frequently an antecedent history of trauma, weakness, and atrophy of muscles. The deformity of Pott's disease is angular in type and usually in the dorsal region, associated with compensatory lordosis. In spondylitis deformans the deformity is not angular, but is a kyphosis, "an extensive and a true curve," associated with a loss of the normal lumbar lordosis; and the head is usually sunken upon the chest instead of being thrown back, as in Pott's disease. Paralysis may occur in both; it is peripheral in spondylitis deformans, but central in spondylitis; it is regular, unilateral (usually), and develops irregularly in the deformans type (Goldthwait). This irregularity is explanied by the irregularity in growth of the exostoses and other bony growths. A family history positive to tuberculosis is of diagnostic value, as is also a tuberculous lesion elsewhere in the patient. In tuberculosis other joints are seldom involved or exostoses found. The diagnosis may be made more certain by the tuberculin test.

2. Pachymeningitis is usually more acute in onset; the stiffness is confined to the cervical region as a rule; there are marked mental symptoms, and the joints of the body are not involved.

3. Occupation kyphosis occurs in those of stooping occupation and does not present joint complications, pain, or exostoses.

4. The strange disease hysteria, which can simulate any known disease, may give many of the symptoms of spondylitis deformans, particularly the pain and the spinal rigidity. The use of an anæsthetic will enable us to determine at once the true nature of the disease. The magic of hysteria has no charm over the power of the anæsthetic. Mobility under ether makes the diagnosis of hysteria.

5. Osteitis deformans of the spine.[5] This is even rarer than spondylitis deformans, is associated with deformity in the long bones, enlargement of the bones of the calvarium, a broadening of the pelvis, and is not associated with exostoses.

Prognosis. This depends largely on the stage in which the disease is recognized. As in tuberculosis, the earlier the recognition, the greater the chances of arrest or cure. When the osseous changes have once taken place we are powerless, as far as restoration to normal conditions is concerned. Early diagnosis enables us to prevent much deformity, if not to arrest the disease itself. There are some dozen cases in which the patient has been greatly relieved, if not cured. Goldthwait (1902) reports five cases in which there was great improvement, if no more. Return is probable under exposure or traumatism.

The disease itself does not cause death, but, on account of

thoracic fixation, almost any serious disease of the lung, as pneumonia or tuberculosis, may terminate life. It is said the most frequent intercurrent disease is pulmonary tuberculosis.

As to cure, after bony changes have occurred no well-founded hope can be entertained.

Treatment. The treatment should be both constitutional and local.

The constitutional consists in good, nutritious food, plenty of fresh air and sunshine, warm baths, and tonics, such as iron, cod-liver oil, arsenic, strychnine and the like. The salicylates, except occasionally in relieving pain, fail absolutely. And it is probable that they are contraindicated entirely because of their tendency to upset the stomach. It is claimed that such patients do best in a warm, dry climate.

All sources of toxic material should be removed, constipation corrected, the skin kept healthy by warm baths and massage, the kidneys watched carefully, and all other ailments should be cured, if possible.

The local treatment includes mechanical support to the spine, either plaster casts or special apparatus; electricity and massage, although some say electricity is harmful. In acute cases use a fixed support. Apply a plaster jacket in the best erect posture. This relieves irritation and muscular spasm. It should be remoulded or reapplied as the patient improves. After the acute symptoms have subsided, use a flexible support, as a spring-steel brace or a leather jacket. Strapping is good. Forced movements or strains of the part are to be discouraged, but this is the one place, and the only place, where fixation is not indicated (except in the acute stage). Motion, both active and passive, should be kept up as long as possible, for, if no injury is done, it tends to keep off the dreaded ankylosis. Some have practised immobilization, with the result of ankylosis of several of the large joints of the body. It is highly important that the condition be not mistaken for Pott's disease, where fixation is indicated in order to limit the disease. Massage retards the progress of the disease, relieves pain, aids absorption of effusion, should there be any, and delays fixation. Warmth locally, as baking, often affords great relief.

RESUME.

Definition. A progressive ankylosis of the spine, depending on structural changes in the joints.

Nomenclature. Osteoarthritis of the spine, spinal form of arthritis deformans, rheumatoid arthritis, spondylitis deformans, rhizomelique spondylose (if hip or shoulder is involved).

Historical. Found in mummies, cats, oxen, horses, and gorillas, as well as in man.

Pathology. That of osteoarthritis, a proliferation of cartilage cells and a subsequent absorption of the intervertebral disks, fusion of the vertebræ, ossification of the ligaments, and formation of exostoses.

Etiology. 1. Age: average, twenty-five to forty years.

2. Sex: males, 75 per cent.

3. Exposure to cold and wet.

4. Trauma.

5. Occupation: long-continued hard work.

6. Infectious diseases, as gonorrhœa, rheumatism.

7. Neurotrophic, metabolic, toxic.

Symptomatology. Early: develops gradually. 1. Pain. 2. Stiffness.

Later: 1. Spinal rigidity, from below upward. 2. Spinal deformity, dorsal kyphosis, with loss of lumbar lordosis.

3. Chest and pelvis flat; thorax fixed; abdominal breathing.

4. Gait and position in bed are often characteristic.

5. Weakness and atrophy of muscles, particularly of back, shoulder, and hip.

6. Joint crepitus, but no tenderness or redness, as a rule.

7. Ankylosis of other joints, particularly shoulder or hip.

8. Exostoses.

9. Nervous disturbances, when present, are sensory, as paræsthesia, hyperæsthesia, anæsthesia, etc., and motor, as tremor and increased excitability.

Diagnosis. 1. Pott's disease. Tuberculin test; angular deformity, usually in young; family history; other joints not ankylosed; no exostoses.

2. Pachymeningitis. More acute; lumbar region not involved; mental symptoms; other joints free.

3. Occupation kyphosis. Stooping occupation; no exostoses; joints not involved.

4. Hysteria. Mobility under ether.

Prognosis. Death from intercurrent disease.

Treatment. Supportive; no cure.

Bibliography.

[The references given below are only those which have been consulted in the preparation of this article. A much more extensive bibliography is given in the papers by Ruhräh, Sachs, and Schlesinger. These include the foreign literature on the subject.]

1. International Text-book of Surgery.

2. Ruhräh. American Journal of the Medical Sciences, 1903, vol. xcvi. pp. 864–78.

3. Dulles. Lectures on the History of Medicine. Aristotle.

4. Osler. The Principles and Practice of Medicine. Fourth edition.

5. Packard and Steele. American Journal of the Medical Sciences, November, 1901.

6. Marie. Revue de Médecine, 1898, vol. xviii.

7. Quoted by American Text-book of Surgery.

8. Tyson. Practice of Medicine. Third edition.

9. American Text-book of Surgery.

10. Frazier. The University Medical Magazine, July, 1901.

11. Lectures on Nervous Diseases.

12. Von Bechterew. Deutsche Zeitschrift f. Nervenheilkunde, vol. xv.

13. Oppenheim. Text-book. Fourth German edition, pp. 274, 275.

14. Sutton. British Medical and Surgical Journal, 1895, vol. ii.

15. Goldthwait. Boston Medical and Surgical Journal, 1897, 1899, 1902.

16. Strümpell. Text-book of Medicine. Fourth American edition.
17. Dana. Transactions of the Association of American Physicians, vol. xvi.
18. Osler. Ibid., pp. 687–694.
19. Stockton. Ibid., pp. 691, 692.
20. Sachs and Fraenkel. Journal of Nervous and Mental Disease, vol. xxvii. pp. 1–15.
21. Rotch. Pediatrics. Fourth edition.
22. Boston Medical and Surgical Journal.
23. Centralblatt f. d. Grenzgebiete der Medizin u. Chirurgie, vol. iii.
24. Marsh. British Medical and Surgical Journal, 1895, vol. ii.
25. May. Ibid., 1897, vol. ii.
26. Tbebault. Review in American Journal of the Medical Sciences, 1901.
27. Le Branton. American Medicine, vol. vi.
28. British Medical and Surgical Journal, 1899.
29. McCarthy. New York Medical Journal and Philadelphia Medical Journal, 1905.
30. Sturge. Transactions of the Clinical Society, London, 1879, vol. xii.
31. Clutton. Ibid., 1883, vol. xvi.
32. Lediard. Ibid.
33. Medical News, 1899.
34. Gordon. Medical Record, 1904.
35. Wood. Transactions of the Pathological Society of London, vol. vii.
36. Ogle. Ibid., vol. viii.
37. Sunol. Independencia Médica, Barcelona, March, 1898. (I was unable to find this reference.)
38. Spiller. Journal of Nervous and Mental Disease, vol. xxvi. p. 577.
39. Ibid.
40. Transactions of the Pathological Society of London, vol. xxviii.
41. Centralblatt f. d. Grenzgebiete d. Med. u. Chir., vol. v.
42. Ibid., vol. vi.

BOOK REVIEWS.

Diseases of the Heart. A Clinical Text-book for the Use of Students and Practitioners of Medicine. By Edmund Henry Colbeck, B.A., M.D. (Cantab.), F.R.C.P. (London), D.P.H. (Cantab.). With 43 illustrations. Second edition. Revised and enlarged. Chicago: W. T. Keener & Co.

In the above-mentioned book the clinical side of diseases of the heart is considered in a consise and systematic manner. It sets forth in a practical way the subjects with which it deals. Being the second edition of the work, it has undergone revisions and additions. Controversional matter has been largely excluded, the author's purpose in view having manifestly been terseness and lucidity. In the physiological section it seems to the reviewer that more attention might have been advantageously bestowed upon some of the recent experimental work in this field—*e. g.*, the action of certain ions upon the function of automaticity, the work of Engelmann, Wenkebach, Mackenzie, and others upon conductivity, stimulus production and the like. Under "Pericarditis" we find no mention of Traube's space or Ebstein's angle. The instrumental determination of blood pressure, too, receives but scant notice. Further, we believe that some of the statements made in the book require modification.

On the other hand, the work is to be commended for its clearness and for a number of excellent diagrams, as well as for its system and grouping of subject-matter. G. W. N.

Toxicology. A Manual for Students and Practitioners. By Edwin Wells Dwight, M.D., Instructor in Legal Medicine, Harvard University. Series edited by Victor Cox Pedersen, A.M., M.D., Instructor in Surgery, New York Polyclinic, etc. Philadelphia and New York: Lea Brothers & Co., 1905.

This little volume on Toxicology, one of the Epitome Series, is spoken of by its author as only a brief compendium of the facts in connection with toxicology; in looking at it we find that it is small in size, but in examining it more closely we note that it leaves little to wish for. After a chapter on toxicology in general it contains twelve other chapters, each dealing with poisons of different classes; none seem to be omitted. A number of cases illustrating the different poisons are sprinkled over the book, and at the end of each chapter a few questions are placed to assist the student in reviewing his knowledge of what he has read. For the practising physician, and especially for the student and hospital resident, it is a book that we can recommend. E. L.

Saunders' Medical Hand Atlases. Atlas and Epitome of General Pathologic Histology. By Dr. H. Duerck, of Munich. Edited, with additions, by Ludvig Hektoen, M.D., Professor of Pathology, Rush Medical College, in affiliation with the University of Chicago. With 172 colored figures on 77 lithographic plates, 36 text-cuts, many in colors, and 371 pages of text. Philadelphia, New York, London: W. B. Saunders & Co., 1904.

This new atlas in Saunders' Medical Hand Atlases is indeed a worthy addition to the series. In looking over it we find that the author has contented himself in giving the generally accepted views in regard to the significance of pathologic processes, and where diverging views exist has only cursorily referred to them; as it is more to the student's advantage and practising physician's to be given a true representation of pathologic processes in general than to have conflicting theories expounded, we can only commend the author in this respect. We are told that all the illustrations have been made from original specimens without combining different microscopic fields, and that extraordinary care has been taken to reproduce them as near to perfection as possible; in some as many as twenty-six colors were required to reproduce the original painting. Dr. Hektoen has edited this volume in his usual style, and has added much useful matter. We can recommend the book to all students of pathology, and believe it to be of unusual value to the medical profession in general. E. L.

Practical Massage in Twenty Lessons. By Hartvig Nissen, Instructor and Lecturer in Massage and Gymnastics at Harvard University Summer School; Director of Physical Training, Brookline Public Schools; former Acting Director of Physical Training, Boston Public Schools; former Instructor of Physical Training at Johns Hopkins University and Wellesley College; former Director of the Swedish Health Institute, Washington, D. C., etc. Author of "Swedish Movement and Massage Treatment," "A, B, C of Swedish Educational Gymnastics," "Rational Home Gymnastics," etc. With 46 original illustrations. 168 pages. 12mo. Philadelphia: F. A. Davis Company.

This is a short concise treatise on massage illustrated fully but rather crudely with 46 illustrations. It contains schemes for combining various movements for all the conditions that can be benefited by massage, gives illustrative cases, and throughout is tempered with moderation, and does not claim massage as a panacea. It should help the masseur in outlining his course of treatment, but of course one cannot learn this art any more from a book than any other.

W. P.

The Surgery of the Diseases of the Appendix Vermiformis and Their Complications. By William Henry Battle, F.R.C.S., Surgeon to St. Thomas' Hospital, etc., and Edred M. Corner, F.R.C.S., Surgeon in charge of Out-patients to St. Thomas' Hospital, etc. Chicago: W. T. Keener & Co., 1905.

Perhaps no other organ of the human body has been so much discussed during the last ten years as the vermiform appendix, and the articles and monographs dealing with its diseases still continue to appear. Additions to its literature, however, as the monograph before us, are highly desirable and there should be a great demand for a book such as it. Not only have the authors given us in the twelve chapters the benefit of their wide experience, but they refer to the literature on almost every page, giving American surgeons particularly much credit for exploiting its diseases and their treatment. As this book is written by surgeons, it stands to reason that they have given the surgeon's view the major place, but they have not neglected the views of the physician and pathologist. In addition to the commoner diseases chapters have been added on acute abdominal diseases, carcinoma, tuberculosis, and other affections of the appendix vermiformis, life insurance, etc., thus clearly establishing their right to claim comprehensive knowledge of the subject. The book is thoroughly practical and as such will be useful to the busy physician.

E. L.

Helps and Hints in Nursing. By J. Quintin Griffith, M.D., Ph.D. Family Edition. Philadelphia, Chicago, and Toronto: The John C. Winston Co., 1905.

This book is called a text-book for nurses and a guide for every family, thus endeavoring to serve a double purpose, which had been better accomplished by dividing it into two separate books. It can be recommended to the family, but contains too much that a trained or graduate nurse should know to be of much value to them. Some such work, however, deserves a place in every household, and if occasionally looked into would prevent many of the absolutely inane accounts of various diseases that the physician hears from lay sources.

W. P.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

A SCHEMATIC EYE:

An Instrument for the Luminous Demonstration of the Functions of the Various Parts of the Eye, of Normal and Abnormal Refraction, and of the Application of Glasses in Disorders of Refraction.

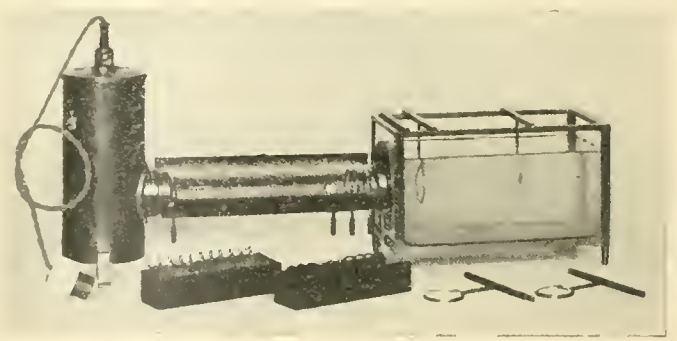
By Edward T. Reichert, M.D.,
Professor of Physiology, University of Pennsylvania.

(From the Laboratory of Physiology, University of Pennsylvania.)

I. General Considerations. In the teaching of physiological optics it has long been recognized that the most effective method is that by which the effects of lenses and their accessories upon the rays of light can be *seen*. Kühne's artificial eye, designed for this purpose, and now in general use, is an optical model of the human eye in the proportion of 12 to 1. It is in the form of a rectangular box, 18 cm. wide, 18 cm. high, and 50 cm. long. The two ends and the front are of ordinary window glass, and the back, bottom, and framework are of sheet metal. Upon the glass of the left end is affixed a lens in imitation of the cornea, and in the box at appropriate places are placed various accessories in imitation of the crystalline lens, iris, and retina. The eye is filled with water in which is dissolved a little eosin or other highly fluorescent substance. The rays passing through this medium can readily be recognized. The instrument is used in a darkened room, the light being obtained from a heliostat, an arc light, an oxyhydrogen lamp, or other powerful source. The rays are so directed as to fall parallel upon the corneal lens.

By means of the Kühne model a number of important phenomena can be shown, as, for instance, the first and second principal foci, the optic axis, the optic centre, the effects of convex and concave lenses, cylindrical lenses and prisms; vision without a crystalline lens; the effects of the functional removal of the cornea, as when the eye is submerged in water; the functions of the iris as regards the effects on the quantity of light and the clearness of vision; the effects of the crystalline lens at rest and in accommodation; Scheiner's experiment, spherical aberration, chromatic aberration, entopic phenomena, etc. Notwithstanding the obvious utility of this apparatus, there remains much to be desired—its cost, its bulk, its weight when filled with water, its liability to leakage, the large lenses and the consequent great danger of injury, the limitations of usefulness owing to structural peculiarities, etc., have of necessity greatly restricted its employment. Owing to such facts the instrument has been modified in various directions, sometimes for the better and sometimes for the worse; but in neither the original nor the modified forms have the possibilities of so valuable a piece of apparatus been developed.

II. Elements of Design of the Schematic Eye. In designing the schematic eye which forms the subject of the present article, the most important problems, apart from the purely mechanical, were those in regard to the light and the lenses. The matter of light has been satisfactorily met in the adoption of an ordinary 16-candle incandescent electric lamp, or a Welsbach burner. The question as to the lenses was of greater importance, and, indeed, constituted the most important to be dealt with. For a number of reasons, especially those pertaining to cost and range of



usefulness, the "test glass" size, and such lenses only as are found in ordinary test sets used by the ophthalmologist, were adopted. This makes it possible for anyone having a test set to carry out a very wide range of observations.

Inasmuch as the eye is schematic, no attempt was made, as in the Kühne model, to retain the proportions of the various parts of the human eye.

The apparatus consists of a *projector*, a *visual chamber*, and various *accessories*. (See illustration.)

The *projector* is formed essentially of two cylindrical brass tubes which are affixed at right angles to each other, the one being in the vertical, and the other in the horizontal. In the former, the lamp is placed and so adjusted that the rays are projected through the horizontal tube into the visual

chamber. The horizontal tube is cut lengthwise in half, one end of the lower part being permanently fastened to the vertical tube, the upper part being hinged to the lower. In the bottom of the latter are provided a number of carriers for lenses and objects. These carriers can be moved to and fro, as occasion may require, by means of handles which project through a slot. After the insertion of the lenses and object, the upper half, or lid, of the horizontal tube may be closed, thus cutting off diffused light that might interfere with observations. This tube is of sufficient length, in conjunction with the lenses selected, to demonstrate the "near" and "far" points, and, of course, all intermediate points in the visual field.

The *visual chamber* is, as in the Kühne model, a tank of parallelogram form, but of much smaller dimensions, and constructed upon much better mechanical lines. The framework is of brass, and the four sides are of window glass. The dimensions are 10 cm. in width, 12 cm. in height, and 25 cm. in length. It constitutes a rigid, compact, and very portable instrument. The rays of light, as in the Kühne eye, can be rendered conspicuous by means of a fluorescent solution. In place of this, smoke is often resorted to. Each has its disadvantages—the former, chiefly in the loss of light; and the latter, in the difficulty, or impossibility, of maintaining satisfactorily during a series of tests a proper degree of density. These objections have been most satisfactorily overcome by a solution of creolin. The visual chamber is filled with water to within 4 or 5 cm. of the top, and in the water is dissolved one or two drops of creolin, which is sufficient to impart a slight milkiness, by means of which the rays of light can readily be traced.

The *accessories* and the problems connected therewith were all carefully studied.

The *field of projection* in the Kühne eye is of ground glass. While this answers satisfactorily, it is far from being all that is desirable, inasmuch as the image can be seen only through the right end of the eye, thus making observation not only awkward, but generally at a disadvantage. Practical experience soon made it manifest that if the image could be viewed from the front, and from above and from the sides, a great gain would be obtained. After experimentation with various devices, it was found that a piece of sheet brass coated with white enamel is ideal. This offers a perfectly smooth, non-transmissive and non-absorptive field. Both sides are enamelled, but on one side, in the centre of the field, is enamelled in yellow a circular area in imitation of the macula lutea, the importance of which will be appreciated in studies of the deviation of the visual axis, and in the application of glasses. One side or the other may be used as may be preferred in the various observations.

The form of the *corneal lens* was given full consideration. If we were to imitate nature the lens should be concavo-convex; but inasmuch as the eye is schematic, and as the lenses used are to be limited if practicable to the test case set, a biconvex lens of appropriate power was selected. In this connection there also arose the problem as to the *best means of causing astigmatism*, that is, whether it would be better to make an exception and depart from the test case set, and to have one or more special astigmatic corneal lenses made, or to make use of the cylindrical glasses of the set. The latter seemed in every way preferable, chiefly because no special and relatively expensive lenses would be required; pedagogically, it seemed that to cause astigmatism by a single cylindrical glass must be more impressive than to have it produced under complex conditions, as, for instance, when the segment of the cylinder is ground on a convex lens; and, finally, the test set makes possible an extremely wide variation in the degree and kind of astigmatism, making easy the production and correction of astigmatic phenomena otherwise almost practically impossible to the ordinary observer.

The method of demonstrating the *mechanism of accommodation* naturally received careful consideration. The photographer, as we know, accommodates his camera to objects near and far by altering the distance between the lens and the field of projection. So simple a plan could be adopted in the schematic eye without departing from what we observe in nature, inasmuch as in certain snakes and amphibia, in osseous fishes, and in cephalopods accommodation is accomplished in this way. Since, however, the especial purpose of the schematic eye is to demonstrate phenomena of the mammalian eye, in which accommodation is effected essentially, and practically solely, by changes in the anterior and posterior surfaces of the crystalline lens, the problem resolved itself into a choice between an alterable lens, such as is used by Fitz in his model to show the effects of changes in the curvature of the lens in accommodation, or two or more lenses of different but properly related values.

The Fitz device is so constructed that the curvatures may be increased or decreased at will, and although very ingenious and satisfactory dioptrically, it is relatively expensive and difficult to maintain in permanent working order. On the other hand, the simple lenses seemed to have almost every feature to recommend them. For general work, two lenses of values to represent respectively the crystalline lens at rest and in full accommodation are all that is necessary. When, however, a test set is at hand, a convex lens of any dioptric value between these extremes may be used, and thus practically every stage of accommodation shown.

In selecting the corneal and crystalline lenses no serious attempt was made to imitate the exact relative dioptric values, but merely to sufficiently approach them so as to give satisfactory illustrations of normal conditions.

The air space and the sheet of glass between the corneal lens and the water of the visual chamber which represents the aqueous humor are departures from normal conditions, but they are not of practical importance in the operation of the instrument.

The *aqueous* and *vitreous humors* are represented, of course, by the water in the visual chamber. To further imitate natural conditions, a movable partition of sheet metal, perforated to admit the crystalline lens, extends across the chamber, thus separating, as it were, the two humors.

The structural features of the *diaphragm* which is to imitate the iris were also studied. Here the choice was between the admirable iris diaphragm so widely used in various kinds of modern optical apparatus, and simple perforated disks of metal. While the former has many desirable and extremely pleasing features, its cost and liability to get out of order under the unusual conditions under which it must be used were strong factors against its adoption. On the other hand, practice has shown that the form answers every purpose with entire satisfaction.

Besides the foregoing there were, of course, many details of variable degrees of importance that had to be considered, but it seems hardly necessary to make specific mention of them.

III. Practical Applications in Physical, Physiological, and Clinical Optics. The schematic eye as thus outlined offers a means for the study of a wide range of optical phenomena, physical and physiological, normal and abnormal. Its adaptability on the clinical side is extraordinary, as is shown by the fact that any disorder of refraction that can be corrected by a test set can be imitated and corrected by the schematic eye. Moreover, one can *see* abnormalities of focusing and their correction. This fact has led me to believe that the instrument will prove of value not only to the student and teacher, but also to the practitioner in the demonstration to patients, in appropriate cases, of abnormalities and their correction.

In the use of the apparatus for teaching purposes it will doubtless usually be found of advantage to study many phenomena of a purely physical character as an introductory to physiological and clinical optics, as, for instance, the refractive indexes of air, water, saline solutions, etc.; the effects of lenses of various kinds; the effects of diaphragms; focal distances, etc. In furtherance of this end, the visual chamber may be filled with smoke, colored water, aqueous solutions of various densities, glycerin, oils, etc. Moreover, by varying the position of the projector in relation to the visual chamber, the rays of light may be caused to fall at any angle upon the refractive medium in the chamber, by simple means of which differences in refraction may be beautifully shown.

The apparatus has been used for the past year in our laboratory and class teaching with great success.

TUBERCULOUS PERITONITIS. A STATISTICAL REVIEW.[1]

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As early as the beginning of the nineteenth century Bichat, Laennec and others had described anatomically this form of tuberculosis. It was not until 1825, however, that the interest of clinicians was aroused by Louis' dictum—chronic peritonitis is usually of tuberculous type. Voluminous literature is at hand, but the object of this paper is to discuss only the statistical side.

It might be well in way of introduction to consider the types of tuberculosis of the peritoneum. Osler divides the disease into three classes—an acute miliary, a chronic caseous and ulcerated, and a chronic fibrous tuberculosis. Spillman selects the following groups—tuberculose miliaire aigue, tuberculose ulcereuse, tuberculose fibreuse, pelvi-peritonite tuberculose, tuberculose peritoneo-pleurale. We may conveniently follow the classification of Osler. It is usual to exclude all cases presenting but a few scattered miliary tubercles in the disseminated form of the disease and those showing no peritoneal involvement save miliary tubercles over intestinal ulcers.

The writer has reviewed 3405 autopsy records of the Pennsylvania, Philadelphia and University Hospitals, and the Henry Phipps Institute. Of these 835, or 24.5 per cent., presented some type of tuberculosis. In addition 76 records showed healed tuberculous foci. This figure is a trifle low and certainly does not represent an accurate percentage of such cases. Tuberculous infection of the peritoneum was found in 92 cases, or in 2.7 per cent. of the total, and in 11 per cent. of the cases of tuberculosis. Postmortem statistics are at variance in this instance. The percentages

[1] Read before the University of Pennsylvania Medical Society, May, 1905.

of peritoneal involvement in tuberculosis range from 1.25 to 16.16 per cent. Borschke gives the latter figure, and in 4250 autopsies at the Breslau Pathological Institute (during six years) he found 1390 cases of tuberculous disease, and of these 226 showed peritoneal involvement. Nothnagel has found that tuberculous peritonitis is more frequently encountered in Vienna than in any other European city. The writer found that 24.8 per cent. of all types of peritonitis were tuberculous, the acute miliary form predominating.

Sex. There seem to be differences of opinion as to which sex contributes the larger number of cases. Vierordt found in 24 persons that 80 per cent. were males. In 107 postmortems, 89 were men and 18 were women, according to Sick. In a series of cases Osler noted that 70 per cent. were males. There appears to be a dearth of literature upon this point. Of the author's cases 30 were females and 62 males —a most decided difference in number.

Age. Osler has found the disease most common between the ages of twenty and forty years. Münstermann and Czerny place it at thirty to forty; however, it is common in children, and is often associated with intestinal and mesenteric disease. It is rare in old age—one case dying at the age of eighty-two years. 357 cases were analyzed by Fenwick, Boulland and others—under ten years, 27 cases; between ten and twenty, 75; twenty and thirty, 87; thirty and forty, 71; forty and fifty, 61; fifty and sixty, 19; sixty and seventy, 4; over seventy, 2 cases. According to the observations of Barthez and Rilliet the disease is rare before the fourth year. The writer has obtained the following results: under ten years, 4 cases; between ten and twenty, 14; twenty-one and thirty, 17; thirty-one and forty, 17; forty-one and fifty, 12; fifty-one and sixty, 9; over sixty, 6 cases. After the fiftieth year the males far outnumber the females. The youngest was sixteen months, the oldest seventy-three years. Of the former cases the following are the notes in brief (taken from the records of the Philadelphia Hospital): Case XXII. Female, aged sixteen months, color, white. American. "General miliary tuberculosis of the lungs, bronchial glands, kidneys, spleen, liver, pericardium and intestines. The tuberculous process in the peritoneum was localized to the serous surface of the intestines and of the diaphragm, and was of the miliary type. Caseous nodules were present in the mesenteric glands. The brain contained an excess of cerebrospinal fluid. Numerous minute, grayish tubercles were present over the pia-arachnoid of the convexity and especially about the vessels of the base over the pons and medulla. The lateral ventricles also contained tubercles and were dilated. The walls showed a dotting of innumerable translucent pinpoint ulcerations." Nothing of especial interest was noted in the seventy-three-year-old case. Allbutt states that the fibrous type of peritoneal tuberculosis is most frequent in men and is almost unknown under two years. Hereditary predisposition is not well marked.

Race. It has been said that the disease is more common in the negro than in the white race. Postmortem statistics are meagre. Of 77[1] cases of tuberculous peritonitis found by the writer there were 39 negroes and 38 whites. With regard to nationality the Caucasians were represented by Americans, 53 per cent.; Germans, 23 per cent.; Italians, French, Irish and Armenians constituting the remainder.

In my series of cases 46, or 50 per cent., of them showed generalized miliary tuberculosis. In 107 autopsies upon tuberculous cases in which the peritoneum was affected the lungs were simultaneously involved in 99 cases; the pleurae in 60; the intestines in 80; the retroperitoneal glands in 41; the spleen in 40; the kidneys in 38; the liver and adrenals each in 66 cases (Wood and Fitz). The writer found 77 of the 92 cases showing specific pulmonary lesions.

Allbutt considers that primary tuberculosis of the peritoneum is of doubtful occurrence. Borschke found but 2 of 226 cases; Münstermann, 1 of 46 cases. On the other hand, Osler quotes that many cases showed none but peritoneal infection. In a series of 17 cases, 5 presented this appearance—1 case showing no disease of the mesenteric glands. In a series of 48 cases studied at St. Thomas' Hospital, London, 2 were primary. The writer found the peritoneum alone affected in 3 cases, or about 3 per cent. of the total. In one of the cases hypertrophic cirrhosis was an associated condition.

The great significance of the primary source of tuberculous peritonitis is noted by Pribrom, who states that out of 165 autopsies 87 cases were attributed to intestinal tuberculosis; 65 to pulmonary and glandular disease; 8 to tubal and uterine; and 5 to osseous tuberculosis. Phillips' and Sick's observations are in accord with the above—considering that intestinal disease is the chief source of the peritonitis. In my series of cases 84 per cent. were complicated by pulmonary disease, and 32.6 per cent. by intestinal disease. Of the latter group (30 cases) perforation of tuberculous ulcers occurred in 4 cases. According to Nothnagel tuberculosis of the peritoneum is very frequently due to rupture of caseous mesenteric or retroperitoneal glands. In women genital tuberculosis is commonly the source. The tubercle bacilli infect the peritoneum through the fimbriated extremity of the Fallopian tube. Not rarely do we note extensive ulceration of the tube with rupture. It has been said that in postmortems in females 25 per cent. of the cases of tuberculous peritonitis showed tubal disease. Immermann found the condition present in 7 out of 16 cases. Osler places the percentage at 30 to 40; Sick at 26.

The author's results showed that 40 per cent. of the cases

[1] In 15 cases the race was not indicated upon the report.

had disease of the tubes. Among men but 8 per cent. of the cases showed tuberculous foci in the genitourinary tract. In this group an interesting case was noted at the Pennsylvania Hospital.

Case IX. Male, aged thirty-six years; negro. Tuberculosis of the epididymis, prostate gland, seminal vesicles, urinary bladder. Healed (?) apical pulmonary tuberculosis (bilateral.) "All the pelvic organs removed *en masse*. The tissue about the left ureter is much thickened and the ureter itself is almost hidden from view. From behind the sigmoid flexure yellow pus oozes from the retroperitoneal tissue. Found to be a ruptured ureter. Immediately above the urinary bladder the ureteral wall is much thickened, and the lumen is narrowed to about 5 mm. Mucous membrane is congested and covered with gray granules. 5.5 cm. above the bladder there is a second constriction measuring 2.5 cm. in length and about 5 mm. in circumference. Above this the ureter widens and forms an abscess cavity which opens directly in the retroperitoneal tissue. The wall of the ureter is 1 cm. in thickness and walls are lined with gray necrotic material. The left kidney measures 16 x 7 x 6.5 cm. It is extremely large, somewhat lobulated, and has a boggy feel. The capsule is thick, but strips readily, leaving a pale, salmon-pink, smooth surface dotted with gray and yellow points. On section an enormous quantity of thick yellow pus gushes out and the kidney seems to be converted into a multilocular abscess cavity, the wall of which is formed by a shell of kidney substance which measures 3 to 4 mm. in thickness. . . . . The urinary bladder is very small and contains only a few cubic centimetres of cloudy urine. Cavity is scarcely large enough to contain a walnut. The mucous membrane is thickened, reddened, and in places yellowish-gray and necrotic. Everywhere small yellow and gray nodules cover the mucous membrane." (Dr. Longcope.)

Allbutt thinks that the ulcerous form is most likely to be associated with tuberculous disease of the intestines or mesenteric glands; 12 per cent. of all his cases showed caseous mesenteric glands. In a series of 127 cases in children, studied by Woodhead, 100 presented involvement of the mesenteric and retroperitoneal glands. In 14 cases mesenteric glands were alone involved. Carr and Colemann have found the mesenterics diseased in 54 per cent. and 66 per cent. of their cases, respectively. In tuberculous peritonitis the anterior mediastinal glands, particularly in the first intercostal area, show tubercles, both gray and caseous. The most important lymphatics of the peritoneal cavity drain into these glands. Durham and Muscatello have made especial mention of the adenoid involvement.

The disease of the pleuræ, pericardium and peritoneum developing simultaneously is known as tuberculous serositis. Practically one serous membrane after the other becomes infected. The Paris theses of Moran and Boulland in 1884–85 have dealt at length with this subject. Boulland divides the disease into three groups: (1) Acute tuberculosis with a rapid evolution of disease in pleuræ and peritoneum, usually following disease of the Fallopian tube, mediastinal or bronchial lymph glands. (2) Cases more chronic, with exudation into the peritoneal and pleural sacs, associated with ulceration and suppurative processes. In this pleural disease is usually secondary, or both conditions may follow pulmonary tuberculosis. (3) In this class pleuroperitoneal disease is still more chronic. The tubercles are hard and fibroid and there is likely to be little fever.

In my series of 92 cases, but 6 presented serositis; 21 cases showed acute tuberculous pleuritis without pericardial disease; 8 cases showed pericardial tuberculosis, in one of which tubercles were demonstrable in the myocardium. In this no disease of either pleural sac was found. Eleven cases showed meningitis, and 2 of these showed disease of the spinal as well as the cerebral meninges. In 1 case the pleural, pericardial, and peritoneal serosæ were infected. The choroid plexus was involved in 1 case. Tuberculosis of the choroid plexus has been studied by McCarthy, who found that in 52 autopsies at the Henry Phipps Institute 7 showed disease of that portion of the brain.

Osseous tuberculosis was a complication in 2 of my series of cases. Case XX. Male, aged fourteen years; negro. Tuberculosis of the sacrum, pelvis, fifth lumbar vertebra and ribs, with gangrene of the left lung and pneumothorax. Chronic tuberculous peritonitis, with disease of the mesenteric and retroperitoneal glands and the spleen. Ulceration of the small intestine, with perforation. (Philadelphia Hospital.)

The other case showed disease of the cervicodorsal vertebræ, with prevertebral abscess and involvement of first metatarsal bone, with sinus formation. General lymphadenoid enlargement was noted. But one case of tuberculous disease of the thyroid was observed, and it was a part of a generalized tuberculosis. Tuberculous gastric ulcers were seen in 1 case, associated with a generalized disease, including the bowel. A questionable case is cited. Case XXXVIII. Male, aged thirty-two years; negro. Miliary tuberculosis of the lungs, liver, spleen and kidneys. "There are seen not less than a dozen bodies in the mucous membrane of the stomach, resembling tubercles which have undergone ulceration leaving the centres somewhat depressed. Otherwise the mucous membrane is normal. Liver weighs 2048 gm. The surface shows numerous tubercles and there are not less than fifty cavernous angiomata, the largest of which is about one inch in diameter. The retroperitoneal glands are enlarged to the size of two fists or more." (Philadelphia Hospital.) Three cases of tuberculosis of the thoracic duct were found.

Statistics concerning tuberculosis herniosa are meagre. Lejars, Jonesco, and Bruns have collected 18 cases. Haegler has noted a case in which the disease was primary in the

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hernia. Another has noted 7 cases. The concurrence of hepatic cirrhosis and tuberculous peritonitis is of especial interest, as suggesting that a non-inflammatory pathological process involving the peritoneum may favor the invasion of the same by tubercle bacilli carried from other parts of the system. Rokitanski, Weigert, Grawitz, and others have suggested that the portal stasis in cirrhosis may exert a favorable influence upon the development of tuberculous disease of the peritoneal cavity. Among 13 cases of fatal peritonitis Nothnagel found 2 cases of cirrhosis. Vierordt found 5 in 24 cases. In the author's series (92 cases) 10 showed cirrhosis of the liver.

It might be well to consider briefly the surgery of tuberculosis of the peritoneum with the percentage of cures, etc. König observed that 70 per cent. of laparotomy cases were over twenty years of age. He considers that operation will cure 25 per cent. of them, with a mortality of 3 per cent. Males constitute a very small percentage of laparotomy cases. Lindner found that of 186 patients 11.3 per cent. were men, and considers that the number of fatal cases was greater among men than women. Among children Phocas found that 82 cases out of 118 were cured by operation. Treves has treated the subject exhaustively. His observations are as follows: In the ulcerous type there were 60 per cent. of cures; in peritonitis secondary to disease of the pelvic viscera, 66 per cent. of cures; in the ascitic, 70 per cent. of cures; and in the fibrous type, 80 per cent. of cures. He places the mortality at 2.5 per cent. Winckel says that 75 to 80 per cent. of cases are cured by operation, and allows five years to elapse without recurrence before considering the disease cured. According to Parker-Symes tuberculosis is an indication rather than a contraindication for operation, because the general condition of the patient is in many instances greatly benefited. The proportion of cures seems to be greater in children than in adults, and Curtiss quotes that the cures in the ascitic type amount to 87 per cent., whereas in the dry form it is 83 per cent.

The surgeon finds that females offer the largest number of laparotomy cases, while the pathologist at postmortems finds the reverse to be the case—that the males far outnumber the females. What is the explanation? Many have been made and some are unique. Dr. A. J. Smith suggests that autopsies are made more frequently upon males than females, and upon reviewing a large number of autopsy reports we have found that 60 per cent. of the total were males. MacCallum has described some curious forms of tuberculosis of the peritoneum. I wish to thank Drs. Biggs and Longcope of the Philadelphia and Pennsylvania Hospitals, respectively, for permitting me to inspect their autopsy reports and to report a few of the interesting cases.

Conclusions. Approximately 25 per cent. of all necropsies show active tuberculous foci. 3 per cent. show tuberculosis of the peritoneum. Of the cases of tuberculosis about 10 per cent. show disease of the peritoneum. Of all forms of peritonitis 25 per cent. are tuberculous. Males are more frequently affected than females, in the proportion of 2 to 1. The disease is most prevalent between the ages of twenty and forty years, and these cases represent over 40 per cent. of the total. After the fiftieth year the disease is comparatively rare in the female. Cases are rather more frequent in the negro than in the white race. The most frequent complication is tuberculosis of the lung. Among women genital tuberculosis is responsible for 40 per cent. of the cases. Among men only a small percentage show some lesion of the genitourinary tract. The other serous surfaces are frequently involved, but instances of true serositis number about 5 per cent. of the peritoneal cases. In laparotomies the fibrous form of the disease gives us the greatest percentage of cures, and the ulcerous the smallest percentage. The average mortality is about 3 per cent. Not a few cases undergo spontaneous cure, but the ulcerous form is incapable of such restitution.

Literature.

1. Osler. Tubercular Peritonitis; General Considerations; Tubercular Abdominal Tumors; Curability. Johns Hopkins Hosp. Rep., Baltimore, 1890, vol. ii. pp. 67–113.
2. Spillman. Dictionaire Encyclopedique, Art. Peritonitis.
3. Nothnagel's System of Medicine.
4. Vierordt. Ueber die peritoneal tuberculose, besonders über die Trage ihrer Behandlung, Deutsches Arch. f. klin. Med., Leipzig, 1889-90, vol. xlvi. pp. 369–387.
5. Fenwick. Lectures on Some Obscure Diseases of the Abdomen, London, 1889.
6. Carr. The Starting Points of Tuberculous Disease in Children. Trans. Med. Soc. London, 1894, vol. xvii. p. 288.
7. Coleman. The Distribution of Tubercle in Abdominal Tuberculosis. Brit. Med Jour., 1893, vol. ii. p. 740.
8. Durham. Medico-Chir. Trans., 1897, vol. lxxx. p. 191; Jour. Path. and Bacter., vol. iv. p. 338.
9. Muscatelle. Virchow's Arch., 1895, vol. cxliii.
10. McCarthy. First Annual Report of the Henry Phipps Institute, pp. 57-58.
11. Lejars. Neoplasmes herniaires et periherniaires. Gaz. des hôp., 1889, p. 801.
12. Jonnesco. Tuberculose herniaire, R. de ch., 1891, vol. lxi. p. 185.
13. Bruns. Tuberculosis herniosa, Btr. z. kl. ch., 1892, vol. ix. p. 767.
14. Haegler. Bruchsack tuberculose, Cor. f. Sch., Ae., 1892, No. 24.
15. Wagner. The Concurrence of Cirrhosis of the Liver and Tuberculous Peritonitis. Deutsch. Arch. f. klin. Med., Bd. xxxiv., 1884.
16. Weigert. Die Weg. des Tuberkilgiftes zu den serosen Hauten. Dent. med. Woch., 1883, p. 453.
17. König. Peritoneal Tuberculosis and its Cure by Laparotomy. Centr. f. Chir., 1890, p. 657.
18. Lindner. Deut. Zeit. f. Chir., Bd. xxiv. p. 448.
19. Phocas. La méd. mod., Dec. 3, 1892.
20. Trens. Annals of Surgery, May, 1894.
21. Winckel. Centr. f. Gynaec., No. 38, 1897.
22. Parker-Symes. Med. Record, April, 1898.
23. MacCallum. Johns Hopkins Hospital, Baltimore, vol. xv. p 293.
24. Duckworth. A Clinical Lecture on Tuberculous Peritonitis. Clin. Jour., London, 1903, vol. xxii. pp. 209–213. (July 22d.)
25. Hegar. Genital tuberculose des Weibes. Stuttgart, 1886.

DESCRIPTION OF A CONVENIENT FORM OF CAGE FOR USE IN METABOLISM EXPERIMENTS ON DOGS, AND OF A NEW METHOD FOR THE PRESERVATION OF MEAT USED IN SUCH EXPERIMENTS.

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In metabolism work in general a quantitative collection of the excreta is essential before any accurate conclusions can be drawn from the data secured. When such experiments are made upon human beings the problem is ordinarily comparatively simple. Under such conditions the urine may be easily obtained in fractions passed at intervals, varying in length according to the nature of the experiment. In metabolism work upon the lower animals, however, the conditions are much more difficult to control. It is, of course, possible to collect the urine in fractions by resorting to the use of the catheter, but even by the use of this instrument one is many times uncertain as to whether or not the urine has been removed quantitatively. In our experience we have seen a dog pass at least 50 c.c. of fluid immediately after having been carefully catheterized by one skilled in the use of the instrument. The use of the catheter is also unsatisfactory from the standpoint of the possibility of infection.

In general metabolism work upon the lower animals, where the establishment of nitrogen equilibrium is essential and where the relation between the income and outgo is studied, we believe it to be safer and in the long run more satisfactory to allow the animal to urinate spontaneously and to collect the urine in twenty-four-hour samples through a long period of time. By checking the results of the analyses of these twenty-four-hour samples of urine for any definite period, by the analysis of a composite sample consisting of aliquot portions of each of the daily samples for the period, we believe that absolutely reliable data may be obtained. The author has employed this method with very satisfactory results.[1] In order to insure absolute accuracy in experiments of this kind it is, of course, necessary to employ a form of cage which admits of a quantitative collection of the urine. A very satisfactory form of cage is that recently described by Gies.[2] In our experience with cages similar to this type[3] we have found them defective in but a single particular—*i. e.*, in the device for the collection of the urine. Unfortunately also the type of cage advised by Gies is rather too expensive to admit of general adoption in the great majority of laboratories where metabolism work is done on a large scale. It has, therefore, been our desire to secure a cage, which, while comparatively cheap, should possess all the good qualities of the type of cage mentioned above and at

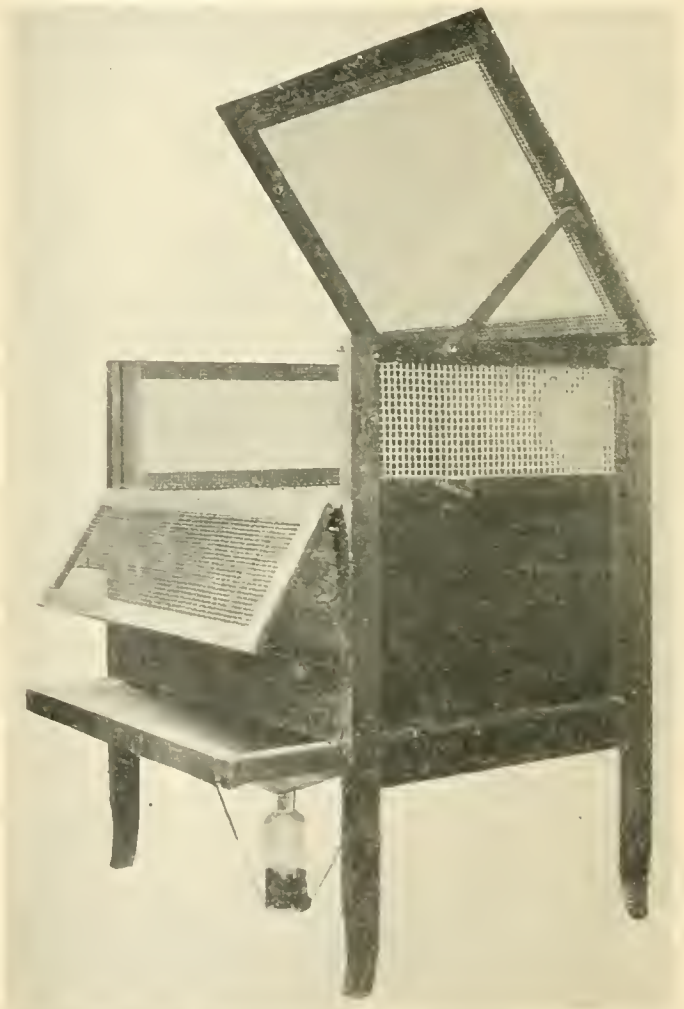

Fig. 1. This figure shows the front and side views of the cage, with the sliding drip pan and its attached device for the collection of the urine drawn slightly forward. The slanting sides of the drip pan are plainly seen. The hinged top and front portion of the cage are open.

[1] Hawk. Proceedings of the American Physiological Society, December 29-30, 1903. American Journal of Physiology, 1904, vol. x. p. xxxvii.

Hawk and Gies. American Journal of Physiology, 1904, vol. xi. p. 171.

Hawk. The influence of hemorrhage upon metabolism. (Pamphlet published in 1904.)

[2] American Journal of Physiology, 1905, vol. xiv. p. 403.

[3] Hawk and Gies, loc. cit.

the same time be provided with an improved device for the collection of the urine. A form of cage has been devised with these two points in view and several of them are now in use in our laboratories and have proven most satisfactory.[1]

Description of the Cage. In practically all forms of cages which are in use for making metabolism experiments upon the lower animals, the metal lining has been zinc. Since this was the universally adopted form of lining for such purposes, we decided to use it in the construction of our cages. However, acting upon the suggestion of Prof. John Marshall we had one of our cages constructed with a tin[2] lining. The coating of this tinned plate is thick and consists exclusively of tin. Ordinary tinned plate has a very thin coating of tin and has minute pin-holes through the tin

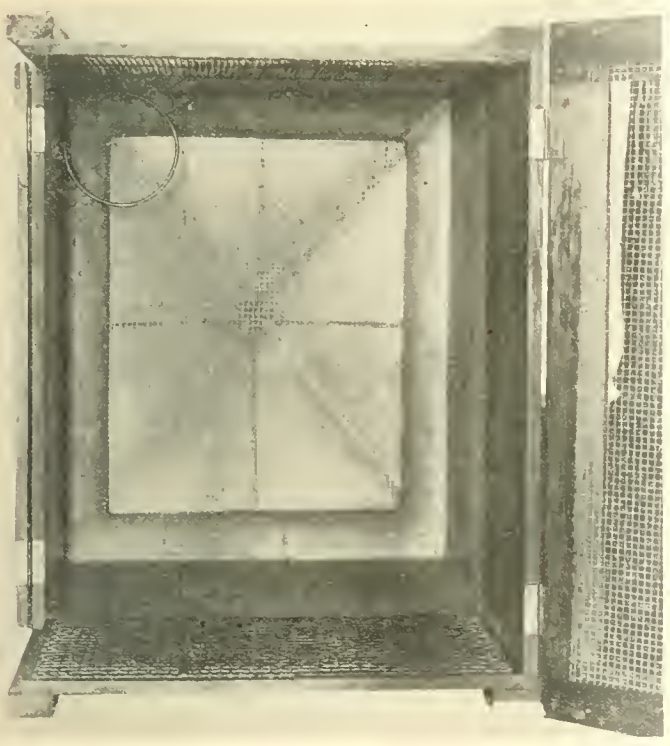

Fig. 2. This figure gives a view of the interior of the cage looking directly down It shows the tin lining with the beveled lower portion, as well as the wire netting bottom and the accompanying drip pan. The removable steel loop for holding the food dish in place is shown in the corner.

coating leading to the iron underneath, thus furnishing ready means for the rusting of the iron. Terne plates are iron sheets coated with an alloy of tin and lead and are obviously unsuited for use in animal cages designed for metabolism experiments. This cage has been in use now for about two years, side by side with cages lined with zinc, and has proven rather more satisfactory than the latter. The tin lining is somewhat more easily and thoroughly cleaned than the zinc and is also apparently less affected by corrosion, etc., due to continued contact with the urine. It also offers another very important advantage, in that the flow of the urine over the tinned surface is much more satisfactory than over the zinc, since a smaller amount of liquid adheres to the metal than in the case of the zinc lining. This is a very important point, since it prevents the formation of any considerable deposit upon the cage bottom due to the incomplete removal of the urine and its subsequent evaporation.

A careful examination of the figures accompanying this article will give a good idea of the construction of the cage. The cage proper consists of a wooden box constructed with a fixed bottom of strong wire netting of about three-eighths-inch mesh. This box is further provided with a tin lining which extends for a distance of eighteen inches above the wire netting, the bottom portion being beveled in such a manner as to assist in the accurate collection of urine should the animal urinate upon the side of the cage. The portion of the cage above the metal lining consists of wire netting similar to that employed in making the bottom of the cage. This side netting should be strong in order to withstand the attacks of an ill-tempered animal, should such a beast, for any reason, be used as a subject. The top of the cage is also of wire netting and is provided with hinges at the back. The portion of the front of the cage which extends above the metal lining is hinged in such a manner as to be readily opened, and in this way facilitates the feeding of the animal and its removal for weighing or for other purposes. A removable steel loop is placed in one corner of the cage, and about six inches from the bottom, for the purpose of holding the enamelled ironware dish from which the dog is fed. In very carefully conducted experiments, where the diet is quantitatively the same daily, it is necessary to give the animal personal supervision at the feeding time, in order that portions of food may not be carelessly removed from the dish and dropped through the netting to the drip pan beneath, and in this way come in contact with the urine at the next urination.

Just beneath the fixed wire bottom, upon which the animal stands, there is arranged a sliding pan of tin, the sides of which slant at an angle of about 30 degrees, thus insuring the rapid passage of the urine to the graduated receptacle beneath. The outlet through which the urine leaves the pan is a tube about one and one-half inch in length and one-half inch in diameter. The upper opening of this tube is closed by means of a gauze of fine mesh which prevents fecal matter, hair and scurf from passing down through the tube and mixing with the urine.

The apparatus for the collection and measurement of the urine consists of a litre graduated percolating jar, whose base

[1] Hawk. American Journal of Physiology, 1904, vol. x. (p. xxxvii. of the Proceedings).

[2] The tin used in the construction of the cages was Gummey's anti-pin-hole tin.

rests within a tin bottom[1] about one-half inch in height, which is fastened to the sliding drip pan by means of three small chains so that the receptacle is suspended in such a manner that its base is about one-half inch from the floor and its top about one-fourth inch from the bottom of the drip pan. The chain fastenings are provided with snaps which hook into small rings securely fastened to the bottom of the pan. To remove the urine receptacle it is only necessary to unfasten the snap nearest the front, thus releasing the tin base and allowing the easy removal of the vessel. If so desired, the opening in the receptacle may be provided with a cork, and in this way loss of urine by evaporation be reduced to a minimum.

The above device for the collection and measurement of the urine we consider to be one of the most satisfactory points about the cage. In practically every form of cage which is used in metabolism work upon the lower animals at the present time, the device for the collection of the urine is not entirely satisfactory. Even in cages provided with a movable drip pan, there is no other device for the collection of the urine, so far as we are aware, which is fastened to the pan in such a manner as to move with the movement of the pan. It was our experience with the old method of collecting urine, by means of a bottle, which was not permanently fastened to the movable drip pan, that there was always danger of forgetting to remove the urine receptacle before drawing the pan, and in this way the risk was encountered of overturning the receptacle and suffering the loss of a valued specimen of urine. By means of the device described above, however, there is no possibility of the loss of a urine sample in this way. With this device, whenever the sliding pan is drawn forward, the urine receptacle is likewise moved forward, and its position in relation to the sliding pan is never altered. It is very desirable to have the urine receptacle graduated, particularly in experiments where data regarding the fractional urination are desired.

The collection of the feces in the old forms of cages used in metabolism work was frequently very unsatisfactory, both in method and result. The animals under experimentation were generally fed an ordinary mixed diet, and the feces from such a dietary were usually of a rather soft consistency and would invariably become mixed with the urine, and in this manner render the analytical data from both the urine and the feces unreliable. By adding bone ash[2] to the other constituents of the diet it has been found, however, that the feces as passed are ordinarily uniformly of such a consistency as to allow of their being removed from the netting bottom by means of pincers or forceps. If a reasonable amount of care is taken to remove the stool as soon after defecation as is convenient, there is very rarely any fecal contamination of the urine. If allowed to remain upon the netting for any considerable length of time, there is always the possibility of the animal stepping or lying upon the stool and in this manner forcing a certain amount of fecal matter through the netting. Of course, with the use of the gauze of fine mesh over the outlet from the drip pan into the urine receptacle, there is no danger of the urine becoming extensively contaminated with feces, except in cases of diarrhœa.

In careful metabolism work upon animals, where the income and outgo of nitrogen, phosphorus, and sulphur are studied, it is quite essential to make a careful collection of the hair and scurf which fall from the body during the experimental period. It is generally customary in experiments of this kind to use only short-haired dogs as subjects, but even with animals of this sort the amount of hair lost during a long period is quite large, and its nitrogen, phosphorus, and sulphur content is not to be neglected if an accurate balance of income and outgo is to be attempted. In cages such as we have described, the hair from the animal will, of course, pass through the netting bottom to the metal pan beneath and may be easily removed by means of a small brush. If it is desired, the scurf may be separated from the hair by the use of a sieve. With short-haired dogs, however, which have been thoroughly washed before being placed in the cage, there is comparatively little scurf given off unless the experimental period be lengthy, and such small amount as must be taken into consideration may generally be included with the hair for analysis.

Method of Preserving Meat. In many metabolism experiments upon dogs, meat is the principal constituent of the diet. When such experiments have for their purpose the collection of data regarding the income and outgo of nitrogen, phosphorus, or sulphur it is obviously most essential that the meat fed from day to day should not vary in composition. In order to obviate any such variation it is customary to prepare, at one time, sufficient meat to feed the animal throughout the whole period of experimentation. The method as suggested by Gies[1] for this preliminary preparation has proven very satisfactory. This consists in first rendering the meat as free as possible from fat and connective tissue. After this has been done the whole mass is hashed by means of an ordinary meat grinder and the juice thoroughly expressed in a tincture press. The meat may conveniently be enclosed in cheese cloth during the process of pressing. After being thoroughly pressed, the various portions are intimately mixed, samples taken for analysis, and the remainder transferred to the proper receptacles and preserved

[1] The end of an ordinary tomato can is satisfactory for this purpose.

[2] Gies. Proceedings of the American Physiological Society, December 29 and 30, 1903. American Journal of Physiology, 1904, vol. x. p. 22; Hawk and Gies, loc. cit.; Hawk, loc. cit.

[1] American Journal of Physiology, 1901, vol. v. p. 235. Also, Biochemical Researches (Gies and collaborators), 1903, vol. i.

for future use. It has generally been customary, after preparing the meat as above, to make it into small balls and to transfer these to small, wide-mouthed bottles or jars. These vessels were then placed in a cold-storage room and the meat used as needed. It has been found that with this method of preparation meat may be preserved for a long period of time, unchanged in nitrogen content. The only feature of the process which seemed to us unsatisfactory was the custom of making the meat into balls and keeping them in small glass receptacles. Of course, very shortly after the meat has been placed in the cold storage it will freeze solid, and while it is a very simple matter to remove any number of the small balls intact from their receptacle, it is somewhat more difficult to cut off any desired amount from one of the frozen balls while it is still within the glass vessel. This process takes an appreciable length of time and during this time the contents of the jar are in contact with the air. The temperature of the ordinary working room, where the weights of the various constituents of the diet are usually made, being so much above that of the cold-storage room, it takes a very short time for the frozen meat to show signs of thawing, and this of itself may introduce an error. It also occasionally happens, that because of the difficulty in cutting the frozen meat while in the receptacle or because of the desire of the experimenter to hasten the process, the receptacle is broken or cracked and the meat, in excess of what is needed for that particular meal, must be discarded.

Having in mind the rather unsatisfactory process of removing the frozen meat from the small glass vessels, and the attendant risk of accident, we modified the method of preserving and weighing out the meat. This modification has been in use in our laboratories for two years and has given uniform satisfaction. The meat is prepared for preservation according to the method given above, and after being very thoroughly mixed is enclosed in sheets of paraffine paper (suggested by Prof. John Marshall) of suitable size. It is now carefully pressed into the form of a cake of about three-fourths of an inch in thickness, transferred to a large museum jar, sufficient cakes added to fill the jar, which is then sealed and placed in the cold-storage room. The meat freezes in hard cakes, but they are very easily removed from the jar, since the paraffine paper prevents them from freezing to each other or to the surrounding glass. When needed for use, the cake is removed, the amount of meat desired is carefully weighed upon a balance *in the cold-storage room*, and the unused portion returned to the jar in its original paraffine paper covering. The cakes being rather thin are easily cut as desired or may even be broken. In case the amount of meat to be fed at each meal is known before it is made into cakes and wrapped as described, the exact amount needed for the animal for one meal may be wrapped in the paraffine paper covering, and in this way all cutting, breaking or weighing of the meat is rendered unnecessary at the time of feeding. Accuracy is not sacrificed by such a method, since the frozen meat may be removed quantitatively from the surface of the paraffine paper.

A chemical examination of meat, prepared and preserved according to the method described above, has shown it to be practically unaltered as far as the content of nitrogen, phosphorus, and sulphur is concerned, after the lapse of about four months.

We wish to express our thanks to Mr. D. B. Evans for suggestions as to the plans of the cages as well as for the satisfactory manner in which he constructed them.

A COMPARATIVE STUDY OF THE SYSTEMIC ACTION OF POTASSIUM SULPHOCYANIDE.

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Probably there is no product of metabolic activity of which there is more doubt as to origin and systemic action than potassium sulphocyanide. Its almost constant presence in the human economy has given rise to much speculation. Thus it has been stated that its effect is similar to that of the cyanides, differing from them in but one respect—namely, that it is less toxic; others have claimed for it an antiseptic action, and at one time indications seemed to point to the possibility of a curative action in tuberculosis; and still others believe that it is an excretory product, being one of the substances produced by the breaking down of proteid. The general consensus of opinion at present seems to lean strongly toward the latter view.

This peculiar substance, having the formula KCNS, may be detected in appreciable quantities by adding to a specimen of human saliva a few drops of acidulated ferric chloride solution. This produces a claret-red reaction which disappears when mercuric chloride is added. A still more delicate reaction is obtained by adding iodic acid, in the presence of starch, to the saliva. The acid is broken down by the salivary salt and iodine is liberated, which in turn causes the starch to become blue. For clinical purposes the ferric chloride

test is the more valuable, as the iodic acid decomposes very readily.

For a long time it was believed that this substance was formed exclusively by the salivary glands, the most active of these being the parotids, but Nencki and Schoumow Simsnowski[1] found it in measurable quantities in the stomach contents of a dog, in which the connection between the mouth and stomach had been previously severed, and Muck[2] demonstrated its presence in the nasal and lacrymal secretions of most of the forty patients examined. These observations seem to show that other body structures than the salivary glands are instrumental in the formation of potassium sulphocyanide. Nevertheless, it is true that normally this substance, which is swallowed with the saliva, is absorbed into the general circulation and reaches all parts of the body; therefore it may be reasoned that it is, in consequence, present in all body secretions, but Leared[3] was not able to find it in cows' milk, sweat, or pus from a cyst; nor has it been detected in bile, pancreatic, or intestinal juices. Therefore its presence in the lacrymal and gastric secretion points strongly to the origin of this substance at least in the gastric and lacrymal glands. Still these observations do not alter the fact that practically all the sulphocyanide is formed in the salivary glands.

Bruylants[4] states that most of the salt is destroyed in the body. Lang[5] was able to recover only one-sixth of that introduced into the body of a dog from the urine. But the more recent researches of Pollock upon dogs, rabbits, and men show that practically all is eliminated by the kidneys. It is possible that during the period of lactation a small quantity may leave the body with the milk, for it was found present in this secretion by Musso,[7] although it may be mentioned that Leared,[8] who made repeated examinations of cows' milk, was unable to demonstrate its presence. Again, a small amount may leave the body by the alimentary canal. Albert[9] found it in considerable quantity in the feces of animals which had been previously given this salt, but there seems to be no data concerning its presence in feces under normal conditions.

When potassium sulphocyanide is taken into the economy, it is not entirely eliminated for several days. Munk[10] noted that after the ingestion of 15 grams of ammonium sulphocyanide the substance appeared in the urine in ten minutes. The reaction increased until the end of the third day, then gradually decreased, but traces could still be found on the seventh or eighth day. He explains this peculiarity of elimination by assuming that some of the salt is readily absorbed and excreted, whereas another portion combines with the organic atomic complex, and when this is broken down the substance is again liberated and may then be readily eliminated. If this theory is true, it is probably that this combination occurs in the liver. Certainly the liver is the organ in which most of the salt is stored after intravenous injection. In three dogs experimented upon in this laboratory it was found when the animals were killed at intervals varying from two to six hours after the introduction of large doses of sulphocyanide into the external jugular vein, that most of the substance was in the liver, much less in the spleen, and very small amounts in the salivary glands.

With few exceptions potassium sulphocyanide is a normal constituent of human saliva. In children, in the first month of life, it is absent, as shown by Pribram and Ritter,[11] but in the adult it is present in at least 90 per cent. of all cases. In the lower animals much contradictory evidence is recorded concerning its presence in, or absence from, the saliva. Gscheidlen[12] found it in the saliva of all of the domestic animals that he examined. Jacubowitsch[13] records its presence in the parotid of the dog, horse, and sheep, as did also Mitscherlisch and Gmelin,[14] but Grober[15] made watery extracts of the salivary glands of the dog, guinea-pig, and cat, but did not obtain a positive reaction. I. Munk[16] maintained that it is absent in the saliva of the dog, and Ellenberger[17] claims that it is not present in the horse, ox, sheep, goat, and pig. This disagreement may be explained by the fact that in these animals its presence is not constant, and when present it is in quantities which need not be considered. Therefore it is only in the human being that this substance has any significance.

The average daily amount of sulphocyanide taken into the system is greater than generally supposed. Grober,[18] who averaged the percentages found in human saliva by Frerichs, Jacubowitsch, Hammerbacher, Vierordt, Tigerstedt, Bruylants, Munk, Kruger, and himself, found it to be 0.088 part in 1000. The quantity of saliva secreted daily varies considerably. According to Bidder and Schmidt,[19] it varies from 1000 to 2000 grams, but many investigators estimate the amount to be considerably less than this. Langley[20] states that "it is generally supposed that the total quantity exceeds a litre a day." If it is assumed that a litre is the daily quantity of saliva secreted, it may be readily seen that 0.088 gram of potassium sulphocyanide is ingested. It is certainly true that frequently this quantity is greatly exceeded, both under normal and pathological conditions. Thus excessive salivation may increase the amount absorbed by the system, but this is not as great as may be presumed. The experiments of Grober, Longet, and Schneider have conclusively proven that prolonged salivation reduces the percentage present in the saliva. The latter experimenter[21] reports an instance where the saliva was continually provoked by chewing soft parafline for three and three-quarter hours, with a reduction of the potassium sulphocyanide from 0.004 per cent. to 0.002 per cent. This reduction may be explained by the fact that normally the parotid gland is most active in the production of this substance, but when

the salivary glands are stimulated reflexly, as shown by Bernard, the submaxillary gland secretes about twice as much as the parotid. Notwithstanding this, excessive salivation increases to a marked degree the quantity of KCNS ingested.

It has been believed by many investigators that other physiological conditions increase the amount of salt in the saliva. The emotions were supposed to increase the quantity, and particularly anger, as stated by Eberle,[22] but this has been denied recently by Grober.[23] Again, it has been claimed that the excessive ingestion of proteid increased its production, but the latter experimenter also disproved this, but recognized the fact that the quantity is dependent upon the albumin katabolism in the system. Considerable discussion has occurred in consequence of the statement made by Bernard that this substance is increased by smoking. This phase of the subject has been thoroughly studied by Krüger,[24] who confirms his statement, but this again is denied by Grober, and it seems that the more general opinion is that tobacco has little or no influence upon the quantity secreted.

Many pathological conditions cause the amount of sulphocyanide to vary to a considerable degree. The subject was first thoroughly investigated by Fenwick,[25] and as the result of the study of a great number of cases he concludes that "whenever an unusual demand is made upon the nutritive organs of the body by the necessities of the system, and the patient gains flesh and strength, the sulphocyanide in the saliva is found to be increased in quantity, but, when on the contrary a person rapidly wastes from some general disease, the amount of the salt is diminished."

All these facts suggest that possibly under the conditions just mentioned the percentage of this salt may be great enough to produce a detrimental systemic action, for it is known that large doses produce toxic effects. Florain[26] in a paper read before the Congress in Paris, 1899, directed attention to the poisonous action upon plants. He stated that when seeds were placed in saliva they germinated more slowly than normal, and that when developing plants absorb a few centigrams of sulphocyanide death followed. Similar results were obtained with fully developed plants. It was further learned from experiments performed in this laboratory that the resistive power of different plants varied greatly. Thus, for instance, common daisies (*Chrysanthemum vulgare*) subjected to a $\frac{1}{2}$ per cent. solution of the potassium salt for twenty-four hours exhibited no evidence of its presence, whereas the buttercup (*Ranunculus bulbosa*) under the same conditions withered and died. The results obtained were carefully guarded by the proper control experiments.

The organized ferments resist the harmful action of potassium sulphocyanide much more successfully than plants. At least this is true of the saccharomycetes, which was the only organism belonging to this group subjected to experimentation. The salt was tested by means of Einhorn's saccharimeter,[27] an apparatus which estimates the quantity of sugar present in a fermenting solution by measuring the amount of carbon dioxide evolved, but which may also be used to study the activity of fermentation. The method of procedure was very simple. A 1 per cent. glucose solution, containing yeast, and a known amount of potassium sulphocyanide was introduced into a saccharimetric tube. Fermentation was allowed to proceed and records were made at half-hour intervals of the amount of carbon dioxide evolved. Several tests with different percentages of the salt were made at the same time. It was found that when 10 per cent. was present fermentation ceased in about an hour, but practically no retardation occurred unless the quantity exceeded 5 per cent. These experiments are of interest because they demonstrate that sulphocyanide in quantities found in the saliva, even when it reaches the maximum, has no effect upon the activity of the organized ferments in the alimentary canal. Studies have been made upon the unorganized ferments by Wrublewski,[28] who states that the salivary salt retards both the action of pepsin and rennin.

The effect of the sulphocyanide upon bacteria has received considerable attention. Hungenschmidt[29] and Garnier and Schlagdenhauffen[30] attributed to the sulphocyanide a distinct bactericidal action. Martinotti[31] reported results in 1896 which indicated that the growth of tubercle bacilli in the living body might be retarded and even destroyed by the administration of this substance. He injected tubercle bacilli into the aqueous humor of the eye of guinea-pigs and rabbits, allowed the tubercles to develop, and then introduced sodium sulphocyanide hypodermically. After continuing the treatment for different lengths of time he noted not only improvement in some animals but even disappearance of the lesions in others. However, much contradictory evidence has accumulated. Schlegel,[32] experimenting with the sodium salt in strength varying from $\frac{1}{4}$ to 1 per cent. upon cultures of bacillus of tuberculosis, diphtheria, glanders, and the staphylococcus pyogenus aureus and citreus, showed that the compound had but little inhibitory effect upon their growth, and concluded that it need hardly be considered as a disinfectant. The researches of Martinotti upon tubercle bacilli were repeated with some modifications by Treupel.[33] He injected the bacteria into the peritoneal cavity of rabbits and guinea-pigs, and then gave the former 0.1 gram and the latter 0.01 gram of sulphocyanide daily. His results show that in no instance was there the slightest evidence of a curative action which could be attributed to the salt.

The response of the protista to the presence of this drug has not to my knowledge engaged the attention of investigators in this field of work. To complete the comparative pharmacological study the paramesium was employed.

This animal served the purpose very well, because not only the reactions of the protoplasm but also those of cilia were readily observed. When a culture of the paramesium candatum was introduced into a 2½ per cent. solution of potassium sulphocyanide the organism no longer moved forward, but revolved very rapidly upon its longitudinal axis. These movements lessened very rapidly and death occurred within a minute. In a 1 per cent. solution death occurred in from four to ten minutes, and it required about thirty minutes for a 0.75 per cent. solution to cause detrimental action. Weaker strength solutions have no observable effect. The influence upon the cilia was similar to that noted in the clam, which will be described later.

Under the head of the action of drugs upon mollusca (lamellibranchiata) Lauder Brunton[34] reports the action of sulphocyanide upon these animals. He states that small doses somewhat accelerate cardiac action, and large doses stop the heart in diastole, and if directly applied the effect is permanent. He further reports that the potassium salt diminishes reflex action, but has little effect upon the excitability of the nerves. The mollusca also afford an excellent opportunity for studying ciliary action. For this purpose the gill of the clam was employed. A microscopic preparation was made in the usual manner, and the rapidity of ciliary movement carefully observed. Then, varying percentages of potassium sulphocyanide in clam juice were applied and any change in the rate and duration of ciliary movement was noted. When the strength of the solution was less than 5 per cent. no change was observed except a slight lessening in the rapidity of the ciliary movement. When this strength was exceeded the effect was more marked, and finally when a 10 per cent. solution was applied almost immediate stoppage of ciliary activity followed.

In frogs the minimal lethal dose is 0.5 gram per kilogram of body weight. When large doses are introduced into the dorsal lymph sac the first symptom to appear is increased rate and depth of respiration, which develops almost immediately after injection. At this stage no changes in heart rate were detected. In approximately fifteen minutes weakness appears, particularly in the posterior extremity. This may be readily elicited by stimulating the animal, causing it to jump away. If this is repeated about a dozen times the animal no longer moves, and if placed upon the back will remain in that position a very long while, being too weak to regain its natural position. These were the only symptoms noted when the quantity given was less than that of the fatal dose. When very large amounts are given, for instance, three or four times the toxic dose, an increase of reflex responsivity appeared and in ten to fifteen minutes opisthotonos developed. The convulsions were mostly tonic in character. Paschkis[35] compared them with those seen in strychnine poison. Later a paralytic stage appears with decreased sensitivity of the skin and mucous membrane. Breathing ceased about thirty minutes after injection, but the heart action persisted twice as long. The sciatic nerve responded to electric stimulation long after cardiac arrest.

Claude Bernard[36] considered potassium sulphocyanide a direct muscle poison, being more powerful in its action upon the heart than skeletal muscle. This is in part true, but it surely has also a primary stimulant effect upon the inhibitory mechanism of the heart. This is demonstrated by the fact that the heart beats longer when subjected to the salt if the both pneumogastric nerves are previously cut, as was shown by Setschenow.[37] Further, Paschkis[38] reported that when atropine was applied to a heart which has been rendered quiescent by the drug, rhythmic activity resumes. With reference to the action of the salt upon the nervous system all authorities agree that the increased reflex activity and convulsions are due to stimulation of the motor cells in the spinal cord.

Upon homothermous animals the action of the drug is quite similar to that observed in poikilothermous organisms. The minimal lethal dose is practically the same, and the circulatory, respiratory, and spinal cord action differ only to a slight degree. The warm-blood animals experimented upon were the dog, guinea-pig, rat, and pigeon, and in all instances the nature of the symptom following the injection of large doses was essentially the same. The dog was more responsive to the poisonous effects of the drug when it was introduced intravenously. When 0.1 gram per kilogram of body weight was injected into a large vein it caused immediate and permanent arrest of cardiac action. The effects of smaller doses upon the circulation and respiration were studied upon five animals. The procedure was as follows: The dogs were first slightly anæsthetized, then a tube was introduced into the trachea and a cannula into the carotid artery. The tracheotomy tube was connected with a Marey tambour and the respiratory movements were recorded upon a moving drum. Every precaution was taken to allow the animal a constant supply of fresh air. A blood-pressure tracing was also taken by means of a mamometer connected with the cannula in the usual manner. One-third of the toxic dose caused a marked increase of the respiratory rate and depth, with a distinct rise of blood pressure, but there was no perceptible change in cardiac rhythm. Setschenow obtained a similar rise in pressure both in the curarized animal and when the spinal cord was severed from the brain. Similar effects were produced by giving the animal a second dose; when, however, the fatal quantity is given there is an immediate cessation of heart action with fall of blood pressure to the abscissa (Fig. 1). This was also observed in one animal in which the pneumogastric nerves had been previously cut, and shows that cardiac arrest is not due to stimulation of the cardioinhibitory mechanism, but

rather to a direct action upon the muscle substance. The respiratory movements continue one to three minutes after the fall of pressure. A convulsion usually occurred at the moment of cardiac arrest.

These experiments were repeated upon an animal in which the drug was given hypodermically and intraperitoneally, instead of into the veins. It was found that doses which killed when injected intravenously produced no effect when introduced under the skin, or in the peritoneal cavity. This dose was repeated seven times within two hours without producing the slightest effect upon blood pressure, and it

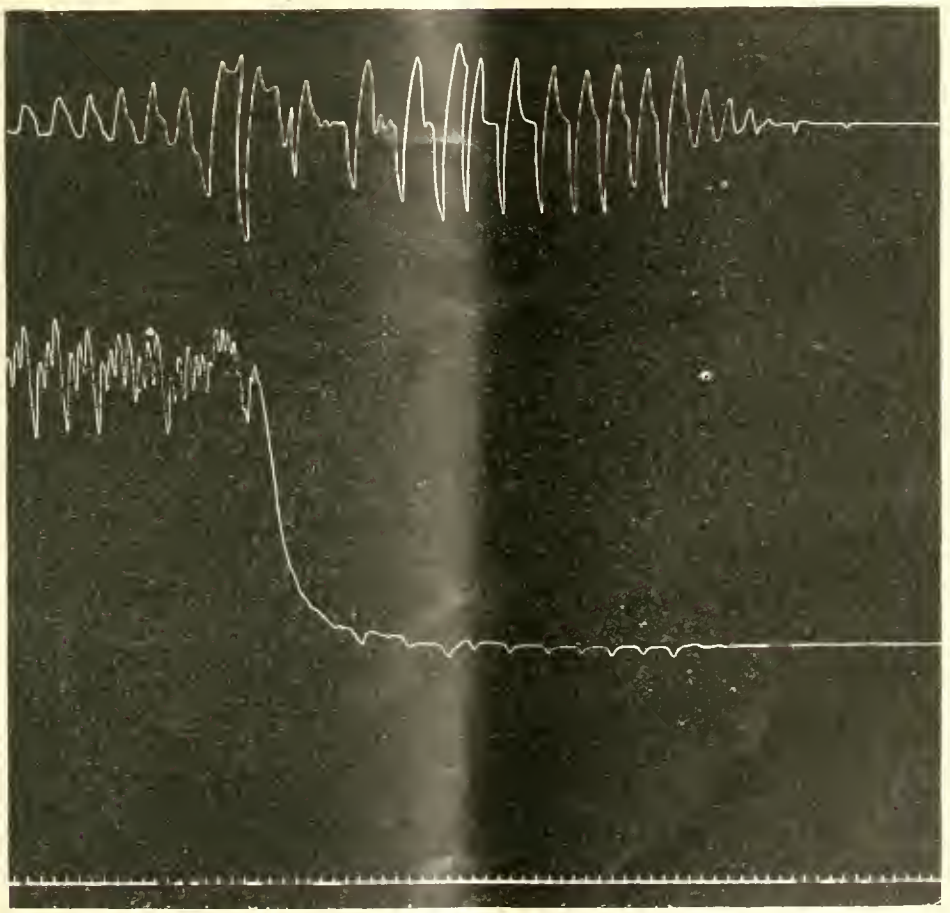

Fig. 1

increased respiratory rate but slightly. The drug acts very slowly when administered by the mouth. When the minimum lethal dose, which was found to be 0.5 gram per kilogram of body weight, was given with the food the symptoms developed very slowly. In one-half to an hour a diarrhœal stool occurred in all four animals. Usually the animals had four or five movements the first day. The diarrhœa was no doubt due to the stimulant action of the drug upon peristaltic movements, as has been recorded by Paschkis.[40] In six to ten hours nervous symptoms appear, the most important of which were unsteadiness of gait, rigidity of the muscles, tremor accentuated during volitional movement, and increased reflex response. Later, clonic and tonic convulsions developed, which have been compared with those produced by strychnine. In addition to these symptoms increased breathing, anorexia, and somnolence were present. Death occurred only after the intravenous lethal dose was repeated on two or three succeeding days.

The effect of hypodermic injections of potassium sulphocyanide was also studied upon the guinea-pig. In these animals the minimum lethal dose was found to be 0.750 gram per kilogram of body weight. The convulsive stage was not marked, but instead paralysis, and particularly of the lower extremities, was the most noticeable symptom.

In white rats similar effects were noted, but the toxic dose was considerably higher, being 1 gram per kilogram of body weight. The pigeon, when large doses were given, exhibited marked ineo-ordination of the wings and legs. However, when just sufficient to cause death was administered, incoordination did not occur, but instead the animal erected the feathers, remained constantly in one position unless irritated, and later exhibited convulsive movements. The minimum toxic dose was 0.5 gram per kilogram of body weight.

These studies justify the conclusion that potassium sulphocyanide is poisonous to all living organisms, both vegetable and animal. It has been stated that the symptoms attributed to this salt are not due to the sulphocyanide, but to potassium. Podcopaew[41] holds this view and maintains that its action as a muscle poison, as believed by Bernard, Kölliker, Setschenow, and Peliken, is due to the potassium. The latter investigator produced death in a dog with 5 grams of potassium sulphocyanide, whereas to another animal he gave 33 grams of the sodium salt with recovery. Nevertheless Mulenberg[42] has shown that when a rabbit is subjected to an atmosphere containing hydrosulphocyanic acid severe convulsions appear in two minutes, and in four minutes death follows. But it is certain that the potassium is far more toxic than the sodium salt, but the fact that the potassium compound circulates in the body lends interest to the study of the action of that salt.

A question of considerable practical value which suggested itself when studying a poisonous action of potassium sulphocyanide was whether or not detrimental systemic effects follow the constant ingestion of small doses. In certain diseases, as first shown by Fenwick, the quantity ingested is greatly increased and the natural deduction is that the constant intake of this poisonous substance in quantities much greater than normal may produce disturbances of nutrition or even pathological conditions. The only experiments recorded which refer to the problem are those which are incidentally made by Treupel and Edinger;[43] when studying the effects of the sulphocyanides in tuberculosis they found that large quantities of the sodium salt could be given over long periods without harmful action. Nevertheless, these experiments in no way indicate whether the more toxic potassium salt is harmless. Therefore in investigations carried out by the writer potassium sulphocyanide was employed. Further, the white rat was used instead of those experimented upon by Treupel—namely, the guinea-pig and rabbit. The advantages that the rat offers are, first, that it is omniverous, therefore its metabolism fairly closely approaches that of the human being; and secondly, because an equilibrium of metabolism can be more easily obtained. Six animals were subjected to experimentation; three were used as controls, and the remaining were given small amounts of potassium sulphocyanide for a long period. The animals were given dog biscuit as a sole article of diet and in quantities necessary to maintain the average weight. Both sets of animals were placed under the same conditions. The rats tested were given 0.006 gram of the drug daily thoroughly mixed with the food. It will be seen by consulting the chart (Fig. 2), which gives daily variations in weight, that the dose is practically eight times that ingested by a normal individual. The experiment was continued fourteen days without any relative variation of the weight of the two sets of animals under observation. The dose was then increased to double the amount and the investigation continued forty-five days longer. It will be observed that the chart shows a slightly greater gain in the weight of the animals given the drug, but the amount is too small to be attributed to this cause. It may be reasoned that the number of animals was too small to give certain results, but the individual variations were quite similar to that of the group and make the experiments more convincing. It may therefore be deduced that it requires much larger doses to produce metabolic disturbances than those normally, or even abnormally, ingested by the human being.

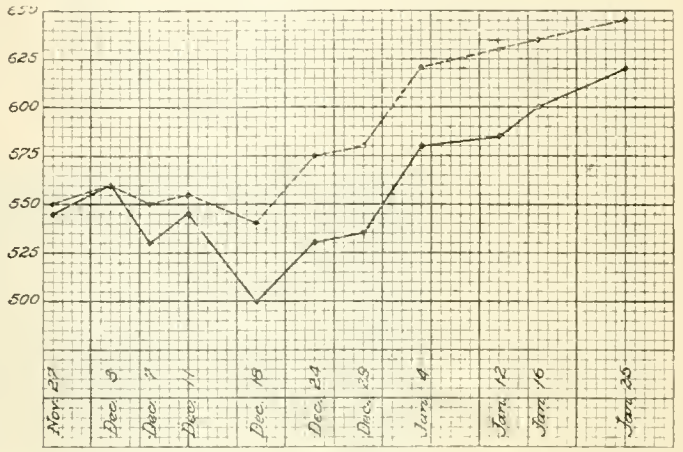

Fig. 2

References

1. Archiv f. Exper. Path. u. Pharm., 1894, p. 313.
2. Munch. klin. Wochenschrift, 1900, p. 1168.
3. Proceedings of Royal Society, vol. xviii. p. 16.
4. Bull. de l'Acad de méd. de Belgique, 1888, p. 18.
5. Virchow's Archiv, p. 69.
6. Hofmeister's Beiträge zur Chem. Phys., 1902, p. 430.
7. Malay's Jahrbericht f. Thierschen, 1877, p. 168.
8. Proceedings of Royal Society, vol. xviii. p. 16.
9. Lancet, 1898, p. 494.
10. Archiv f. Path. Anat., 1877, p. 350.
11. Jahrbuch de Phys. v. Path. d. ersten Kindesalters, 1868, vol. x. p. 148.
12. Pflüger Arch., vol. xiv. p. 401.
13. De saliva, 1848, p. 15.
14. Handbuch d. Org. Chem., 1848.
15. Deutsch. Arch. f. klin. Med., 1901, p. 243.
16. Archiv f. d. ges. Phys., vol. lxi. p. 620.
17. Vergleich. Phys. d. Hausthiere, 1890, p. 495.
18. Deutsch. Archiv f. klin. Med., 1901, p. 243.
19. Quoted in Landois' Phys. d. Menschen, 1900.
20. Schäfer's Text-book of Phys., vol. i. p. 491.
21. Amer. Jour. Phys., vol. v. p. 278.
22. Handbuch d. Verdauung, 1834, p. 28.
23. Deutsch. Archiv f. klin. Med., 1901, p. 243.
24. Zeit. f. Biol., 1899, p. 5.
25. Lancet, 1887, p. 1171.
26. Abstract in British Journal of Dental Science, vol. xxxiii. p. 305.
27. Deutsch. med. Woch., 1888, p. 620.

28. Berich. d. deutsch. Chem. Gezell., 1895, p. 1718.
29. Annal. d. s. institut. Pasteur, 1890.
30. Fremy's Encycl. Chem., 1902.
31. Centr. f. Bach. v. Parasitenk, 1896, p. 142.
32. Münch. med. Woch., 1900, p. 768.
33. Ibid., p. 770.
34. Text-book of Pharmacology, p. 114, 3d edition.
35. Med. Jahr. Wien., 1885, p. 533.
36. Lecon's sur les effects des substances toxique, Paris, 1857.
37. Virch. Arch., 1858, p. 356.
38. Med. Jahr. Wien., 1885, p. 533.
39. Ibid.
40. Ibid.
41. Virch. Arch., 1865, p. 512.
42. Die Schädlichen gase, 1865, p. 474.
43. Münch. med. Woch., 1900, p. 717.

SUGGESTIONS FOR PREVENTIVE MEDICINE IN THE COUNTRY.

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Mr. President and Members of the Lancaster County Medical Society: As a result of your kind invitation to be with you to-day, I venture to invite your attention to a subject that I deem worthy of much more consideration than is usually accorded it, namely, "The Practice of Preventive Medicine in the Rural Districts."

In recent years the possibility of preventing many of the common maladies with which we have to deal has been fully demonstrated. In the large centres of population prevention has become the order of the day, and I know of nothing that contributes more to the honor of the noble profession of which we are members than the fact that the impetus to this work came from medical men; that its evolution is due to the ceasless efforts of medical men; and that its practice is advocated by medical men, even though they are fully aware that the effective exercise of preventive measures operates continually and directly against their financial interests.

Before an audience of this character it would be presumptuous on my part to define the modern conception of preventive medicine, or to detail the stages through which it has passed in the course of its evolution.

That the foundation stones of real and permanent progress were laid in discoveries which revealed to us the nature of many factors capable of exciting disease; that these discoveries began but a little more than a quarter of a century ago, and that with the lapse of each year we find ourselves nearer to the solution of problems hitherto veiled in obscurity, and seemingly surrounded by unsurmountable difficulties, are old stories to you all.

During the past twenty-five years there has been a complete revolution in many of our medical conceptions and methods, with results that more than compensate for all the energy that has been expended.

The most conspicuous growth of this development of modern medicine has, up to the present, been seen in our large centres of urban life—though a partial appreciation of its importance is evidenced from time to time among the rural communities. The reason of this deficiency on the part of those living in the country is not necessarily lack of desire or of intelligence, but often a lack of the knowledge that the fundamental features of preventive medicine are the exercise of simple, common sense based upon data derived from accurate scientific study of the conditions under which we live, and that to do this it is not essential to adopt elaborate or expensive artificial aids.

As I conceive it, the problem of preventive medicine in the country differs from that in the city only in degree. They have the same unit as a starting point—viz., the individual household, and fundamentally they are, therefore, alike in kind, with the prospects of successful solution, *a priori*, somewhat in favor of the resident of the country.

It shall be my purpose in these remarks to indicate in what manner the underlying factors in preventive medicine may be practised in the country and to express the belief that where conscientious care be given to the regulation of certain conditions under which we live, that suffering, sickness, and death may be very much lessened and the common comfort of life very much increased.

At the start we must remember that while the resident of the city has most of the conditions under which he lives regulated more or less satisfactorily for him by experts employed for the purpose, the resident of the country must in most instances take care of all such matters himself, and it is therefore wise to specify at the start the primary factors and conditions on which his physical welfare depends and with which he is daily surrounded that demand his special care.

Food and drink he must have and the waste products resulting therefrom must be disposed of. In consequence his water supply, his dairy products, his vegetables and meat must be considered on the one hand, and the approved methods for the disposal of his excrementitious products on the other.

He should know that many diseases of domestic animals are transmissible to man, and some of those seen in man may be conveyed to animals.

He should know that insects, especially flies and mosquitoes, are active factors for the dissemination and perpetuation of certain types of disease, and he should never forget that if rigid supervision of contagious diseases is good for a city population, it is equally good for those living in the country.

With very few exceptions in country districts human excrement is disposed of in about the same manner as was popular centuries ago. It is deposited upon the soil or in shallow pits to lie there indefinitely without protection from insects, without deodorization or disinfection, until it is convenient or obligatory to remove it. In many instances, it is true, this is but a violation of an æsthetic sense and does no particular harm, but with the advent of disease in the family, if no change be made in the plan, accidents of a very serious nature are likely to result.

As I see this subject, it is not only a health question, but is one of common cleanliness, decency, and comfort that may easily be adjusted by resort to a few simple expedients.

This is neither the time nor place to enter into the details of the manifold ways in which these defects may be eliminated. It will suffice to say that there should never be an accumulation of human excrement for more than a week; that it should be prevented from putrefaction with the consequent odors through the regular use of such desiccating matters as dried loam, ashes, or lime; that in times of sickness, especially bowel troubles, each evacuation should be disinfected before disposed of in the outhouse or otherwise; and that under all circumstances the access of flies to human excrement should be prevented in so far as it is possible.

For elaborate houses having modern equipments there is no better means for the disposal of its sewage than by subsoil irrigation, and for small villages having a common water supply the best means of getting rid of its fluid waste is by intelligently manipulated surface irrigation if the character of the soil admits of it.

Cesspools, pits, etc., in which putrefactive matters accumulate for indefinite periods are a nuisance prejudicial to health and should be eliminated wherever practicable.

Intimately related to the question of the disposal of human and household waste is that of the water supply.

For the country householder this is a matter of the greatest importance, and more or less serious danger from polluted water is only to be eliminated through unrelenting vigilance.

As the majority of single houses in rural districts derive their water supply from shallow wells, it is obvious that the soil in which such wells are sunk should be kept as free as possible from contaminating matters.

The existence of drinking wells and cesspools in near proximity constitute a sanitary trespass that should not be tolerated in any enlightened community. It was just such a state of affairs as this that underlay the prevalence of typhoid fever in Munich in the middle of the last century, and gave to that charming city the reputation of a pest centre. In fact, as was said in speaking of the disposal of excreta, cesspools or any other arrangement for the accumulation of large quantities of decomposable matters in the soil are not only unnecessary and offensive, but actually dangerous.

The drinking well, as ordinarily seen, is very commonly open to pollution by surface washings, as well as to those from the deeper parts of the surrounding soil. This can be in part obviated by building up the mouth of the well by brick laid in cement for at least a foot above the surrounding soil, and filling in around this barrier with earth.

A few years ago an excellent suggestion was made by Koch in connection with open wells in the country—to the effect that they be converted into pump wells by sinking into them an appropriate well pipe and filling in around it with clean fine sand. This sand acts as a filter and to some extent diminishes the danger both from surface washings and pollutions from the deeper layers. The plan converts an open well into what is practically a driven well.

A question of great importance to those dependent upon wells for their water supply is what to do in the event of a well becoming infected. Experiments made upon purposely infected wells demonstrate that it is easily possible to disinfect them providing they can be thrown out of commission for a brief period. The generous use of chloride of lime or carbolic acid in a well, together with the scrubbing of all surfaces with the solution and the repeated emptying of the well, after an appropriate period, until all trace of the disinfectant used has disappeared, results, as a rule, in the elimination of all danger, providing, of course, that the source of pollution has been detected and its action checked.

The care of general water supplies to hamlets, villages, and towns does not concern us; that is usually in the hands of properly constituted authorities.

In certain rural districts, especially those surrounding our large cities, a thriving industry is the raising of vegetables for table use, and a common practice is the fertilization of such vegetables with human night soil derived from the towns or cities. While this is a most excellent plan in so far as fertilization is concerned, it is not a plan that is without objection. While it has been impossible for me to secure direct evidence of the causation of disease through the use of vegetables so fertilized, there is, nevertheless, a very widespread opinion that this is possible, and when we remember that many of the vegetables supplied by the suburban truck farmer are consumed in a raw state, I do not think it needs a great stretch of the imagination to believe that such foods, if surrounded by human excreta during their growth may be a fruitful factor at irregular intervals in the causation of intestinal infection.

Where human excrement must be disposed of in this manner, and often there are no other means for its disposal, its use should be absolutely prohibited until it has been carefully disinfected through the generous admixture of lime. Experiment has shown that fecal matters, while not necessarily rendered sterile, may nevertheless be robbed of their dangerous infective ingredients through the admixture of freshly burned lime in the proportion of 2 per cent. by volume.

During the past few years a great deal of energy has been expended in the study of insects in their relation to the dissemination of disease. As a result we know that certain types of disease, especially malarial and yellow fever, depend for their existence solely upon the activities of mosquitoes; that certain other blood-sucking insects may cause other specific infections in man and in animals; and that many of the non-blood-sucking winged insects that are commonly seen about the habitations of man, especially the common house fly, may serve, mechanically, as carriers of infective matters from the manure pile or cesspool into the dairy or pantry unless prevented by appropriate means from doing so.

Aside from the question of disease, common comfort demands the destruction of the breeding places of mosquitoes and flies and the prevention of their access to the household. The studies of these insects have contributed much that is new to our knowledge of them. We know that the most insignificant collection of water serves as a hatching place for the eggs of the mosquito, and that under normal conditions four or five broods of young may be hatched in a season. We know from actual experiment that fresh horse manure is the most favorable nidus for the propagation of the common house fly. These facts teach their own lesson. No useless accumulations of water should be permitted if it is possible to empty them out or drain them away. If drainage cannot be practised, oil should be spread upon the surface of all pools once in three weeks in the proportion of a teaspoonful to the square yard. Oil thus spread on the surface of a pool containing mosquito larvæ is drawn into the trachea of the developing insect when it comes to the surface to breathe, with instant strangulation as the result.

Horse manure should never be piled openly and exposed about the premises. It should be stored in covered pits or carted away and spread upon the land.

The most conscientious attention to these matters can result only in a diminution at their source, consequently every opening to a house in the country should be carefully protected by screens. I need not ask you what would result from a fly getting into your pantry or dairy after having been feeding upon an undisinfected typhoid evacuation.

Not only in the country, but everywhere, the fly screen and mosquito net are important aids in preventing the spread of disease. Every patient suffering from a transmissible disease, of such nature that the infective particles are given off by way of the excretions should, during the season of insect activity, in addition to the routine disinfection of such excretions, be treated under a mosquito net.

In addition to the foregoing precautions that aim in the main to the prevention of disease and discomfort in the individual household, there are others that should be considered seriously by those residents of the country who are engaged in the production of milk and other dairy products. These necessities of life are peculiarly adapted to the conveyance of disease, and unless they be produced with the greatest care they become disseminators of infection second to none with which I am acquainted.

During the past few years sanitarians have given to this subject a great deal of attention with the result that much improvement is seen in the methods of this industry, but there is still room for improvement, and I do not believe the ideal condition or anything approaching it will be reached until the farmer is educated in the correct methods of his work; until by law he is forbidden to engage in the business unless equipped to properly conduct it, and until it is demonstrated to him that the production of milk, butter, and cheese under approved methods is a better business proposition than where those methods are ignored.

The sanitary control of the dairy should proceed from three standpoints:

1. The production of clean milk with good keeping qualities.

2. The production of milk that conveys no disease from the cow to the consumer.

3. The production of milk under such conditions that it does not serve as a vehicle for the conveyance of disease from one human being to another.

The production of clean milk is not only æsthetically desirable, but is of direct monetary and sanitary advantage. A dirty milk, be the dirt specifically infective or not, does not keep and is an indication of both ignorance and carelessness in the conduct of the business; in brief, the production of unclean milk is bad business, and with the growing demands of an enlightened public for milk properly produced, its continuance daily becomes worse business.

Its correction needs no elaborate outlay. Clean, well-ventilated and lighted stalls, clean cattle, absence of accumulated manure in the stable yard, clean hands and clothing during milking, clean utensils, and a cooling place free from dust are the fundamentals to success.

The production of milk that conveys no disease from the cow to the consumer depends entirely upon the condition of the animal. I fear the interest in the relation of tuberculosis of animal origin to the users of dairy products has so overshadowed all other considerations in this connection that certain other possibilities have almost been neglected.

While I would not, even if I could, minimize the importance of excluding from milch herds all tuberculous cattle, still I must insist that there are other very common disease conditions of cattle, generally regarded as of but little moment, that are a grave menace to the health of those using the milk of such cattle. I refer in particular to non-specific inflammations of the udder. Some years ago my attention was directed to certain acute intestinal troubles, especially occurring in children, that seemed to depend upon the milk fed to them. An investigation of the matter revealed the fact that in many cases the milk given to these children contained the common pyogenic cocci, particularly the streptococcus. On looking further into the matter we found that often one or more cows in the herd from which that milk came were suffering from varying degrees of mammitis, at times so insignificant as only to be detected by microscopic examination of the centrifugated milk or by careful examination of the animals by expert veterinary surgeons.

The outcome of the matter is that in the laboratory of the Board of Health of Philadelphia the examination of milk for pus and pus organisms has become a routine procedure. All milk in which these elements are found is excluded from the market until a competent veterinarian certifies that the diseased cow or cows have been found and excluded from the herd, and until repeated examinations of milk from that herd show it to be free from the objectionable ingredients.

To illustrate the trustworthiness of this method we have discovered such disease-producing milk from four hundred different herds, and in over 85 per cent. of the cases the diseased cattle were detected without difficulty. The influence of this procedure on the care exercised at the source of production is well illustrated by an experience during 1904, when the condemnations for pus and streptococci fell during a period of ten months from 7.7 per cent. to 0.1 per cent. in an average of 757 samples examined monthly, or a total of 7570 for the whole period.

I do not believe that anything we have done toward improving the character of our milk supply has had a more beneficial influence than this particular examination. That it is possible through microscopic examination of a sample of milk found in the city to secure evidence through which a diseased cow may be identified in a herd miles away has impressed many of the producers as close to magic, and we have lost none of their respect through it.

The production and distribution of milk under conditions that eliminate it as a vehicle for the conveyance of disease from one human being to another is a matter having to do with the health of those concerned in the production and distribution of milk.

We do know that certain diseases of man can, and we do not know which cannot, be conveyed through the agency of milk, and so long as we are in this state of ignorance the conservation of the public health demands that we shall assume such conveyance to be possible for all diseases. In consequence no one not in sound health should have anything to do with the milk industry. It is needless for me to call your attention to the instances in which the acute specific infections, such as diphtheria, scarlet fever, typhoid fever, etc., have been disseminated from farms on which a case or cases of the disease existed. It is equally probable that a consumptive milker or handler may and has contaminated milk with matters coughed or spat up during the course of his work, and it is quite certain that milk as well as the udders of cows are often infected from the milkers having upon their hands inflammatory conditions, perhaps not of themselves serious, but still containing micro-organisms which, having found access to the milk, may render its use a very serious matter to the consumer.

This brief sketch of the sanitary requisites of the dairy obviously indicates that more care must be given to this important factor in preventive medicine than has been the case in the past. It calls for nothing, however, that is unreasonable or illogical; it is simply a common-sense demand that is the outgrowth of our increased knowledge on the subject.

In so far as the management of contagious diseases in the country is concerned, there is as yet no uniformity in the methods. In a number of States it seems to be done with something like system, in others they get no attention whatever. Many of our States are properly proud of their systems of registration, but so far as I can see from an examination of their results they are of much more value to the student of demography than to him interested in the prevention of disease.

If it is essential to the correct administration of preventive medicine in our cities that every case of contagious disease be reported promptly to those in authority, it is equally important that the same be done in the country. Were this a common practice the serious local outbreaks of acute contagious diseases so often seen in country districts could be prevented or controlled before they had reached alarming proportions. If it is of advantage to compel the isolation of such cases in city homes and to disinfect such houses at the termination of the disease, and I doubt if any of my hearers question the advisability of such precaution, I maintain that it is equally important in the country districts. In many cases, I am glad to say, this is done, but in most of them it is on the initiative of an intelligent private physician and not as a regulation of a properly constituted body that reaches all cases.

I maintain that the location of contagious diseases throughout the rural districts should be definitely known and officially published at frequent intervals, just as is done among the urban populations, and that the public should be warned

of all houses in which such diseases exist. A case in point may illustrate the necessity for this plan. While on a visit to the country recently I met a funeral train on the road and was told that a very fine young farmer had contracted "tonsillitis" from his father and had died from it in less than forty-eight hours. Within two or three days of the death of the young man the attending physician had three children ill in adjoining houses, all suffering also from "tonsillitis." From two of the houses in which these children were located milk was being regularly shipped to a city some miles away. On inquiry I found that nothing had been said of the necessity of isolating the cases; no warning had been given to the parents; nothing had been said to the neighbors about the possible danger from these cases. The whole matter was in the hands of the doctor, and so far as I could gather there was no official investigation or supervision of the condition that was likely at that time. I do not believe such a condition possible in any of our large cities to-day.

During the latter part of the year 1903 my attention was attracted to an unusual number of cases of typhoid fever in a circumscribed area of Philadelphia. Investigation revealed the fact that in the family of the dairy farmer supplying the milk to the district five out of seven souls had been down with typhoid fever at a time that would satisfactorily account for the outbreak in the city, yet not one of the cases had been reported to any one in authority.

The dependence of our cities upon the surrounding country for many food commodities demands that we should have a knowledge of the location of all outbreaks of contagious diseases in our States. With such knowledge in hand, appropriate steps toward the isolation of cases and removal of the cause of the outbreak can be taken.

Wherever the practice of public preventive medicine has been taken seriously the greatest assistance has been derived from the routine medical examination of school children. The exclusion from school of all children suffering from acute ailments of whatever character, until the true nature of the disease can be determined, has prevented many widespread outbreaks that would have necessitated our doing in the city just what is so often done in the country—namely, the closing of the school, not to mention the suffering and possibly the deaths that were prevented.

I am not prepared to offer a plan, but I do believe that if the conscientious medical supervision of school children in the cities is of advantage to the public health, it would prove of equal advantage if put into operation in our rural districts.

The value of antitoxin in preventing diphtheria; of the bacteriological examination of suspicious sore throats, and of vaccination in preventing smallpox are established facts. They are preventive measures without which little or nothing can be done in controlling the respective diseases, and should be so regarded by all central State authorities. They should be available without cost to all who are unable to pay for them, and every practitioner should be encouraged to give to his patients their full protective benefits.

The more one sees of contagious diseases in the cities, the more convinced does one become that properly equipped hospitals are necessary for their safe conduct. Every infected private house may properly be regarded as a possible focus of dissemination. In few private houses can contagious diseases be managed without danger to those in near proximity to them. If you will think for a moment of the every-day life of the private household, the comings and goings, and the lack of appreciation of the essentials to complete isolation, you will, I think, agree with me that a multiplicity of such foci in a community is a serious obstacle to the prevention of disease.

Contagious diseases should be segregated in properly equipped and efficiently manned hospitals. Such hospitals should provide for the reception of all cases in the community, not only those who are unable to pay for their care, but they should offer private quarters for citizens more fortunately circumstanced who prefer to be treated by their own physicians in consultation with the hospital staff.

With such additional common-sense precautions as are appropriate to conditions not often found in the cities it is obvious to you, from what has been said, that I believe preventive medicine in the country is only to be put into successful operation through the adoption of most of the features peculiar to the work as practised in the cities.

If you agree with me in believing this desirable, then the paving of the way for it must begin with the education of the people, and there are none whose opportunities for good in direction are superior to those of the general practitioner of medicine.

BOOK REVIEWS.

Clinical Methods. A Guide to the Practical Study of Medicine. By Robert Hutchinson, M.D., F.R.C.P., Assistant Physician to the London Hospital and to the Hospital for Sick Children, Great Ormond Street, and Harry Rainy, M.A., F.R.C.P. Ed., F.R.S.E., Examiner in Medicine and Clinical Medicine, St. Andrew's University; formerly University Tutor in Clinical Medicine, Royal Infirmary, Edinburgh. With upward of 150 illustrations and 9 colored plates. Ninth edition. Chicago: W. T. Keener & Co., 1905.

This pocket-size book in the English style contains chapters on Case-taking, General Condition and Appearances, Alimentary System and Abdomen, Circulatory System; Clinical Examination of the Blood, Respiratory System, the Urine, the Skin, Nervous System; Examination of the Eye, Ear, Throat, and Nose; Locomotive System; the Clinical Examination of Children; the Examination of Pathological Fluids; Clinical Bacteriology.

In truth a venturesome collection of chapters to be included in such a handy little volume; but they are well and fully written, up to date, and well illustrated. We would recommend the chapter on the Clinical Examination of the Blood as a concise and well-selected article. In fact the parts treating of the clinical-laboratory methods appeal to us more than those devoted to physical diagnosis, though we have no real criticism to make of these at all, and the chapter devoted to the clinical examination of children is excellent. On the whole, the book is to be commended and should prove useful; the number of editions it has passed through shows the reception it has met with from the public. W. P.

Clinical Treatises on the Pathology and Therapy of Disorders of Metabolism and Nutrition. By Professor Dr. Carl von Noorden, Physician-in-Chief to the City Hospital, Frankfurt a. Main. Authorized American translation. Edited by Boardman Reed, M.D.; translated by Florence Buchanan, D.Sc., and I. Walker Hall, M.D. Part VII. Diabetes Mellitus, its Pathological Chemistry and Treatment. New York: E. B. Treat & Co., 1905.

The seventh volume of this series deals with the author's views on the pathological chemistry and treatment of diabetes as expressed in a series of lectures before the graduating class of Bellevue Medical College, New York. Von Noorden, probably more than anyone else, on account of his thorough knowledge of the physiology, chemistry, and pathology of the disease, obtained from the enormous clinical experience gained from patients at hospitals and sanitaria, is qualified to acquaint us with the latest discoveries and conclusions concerning the origin, complications, and dangers of the disease, as well as to tell us the most successful methods of avoiding and combating them, and he has well acquitted himself of the task. The treatise is a credit to the author, to the translators, to the publisher, and to the physician who owns a copy of it.

We especially wish to call attention to the tables regarding foods which may be consumed by diabetic patients having the different grades of the disease, and which if adhered to will save much suffering to the patient and be a source of satisfaction to the physician who prescribes them.

E. L.

Hygiene and Public Health. By B. Arthur Whitelegge, C.B., M.D., B.Sc. Lond., F.R.C.P., D.P.H., and George Newman, M.D., D.P.H., F.R.S.E. Tenth edition, revised, enlarged, and in great part rewritten; illustrated. Chicago: W. T. Keener & Co., 1905.

This work on *Hygiene and Public Health* is well known to us, as also to the rest of the medical profession, for several years past in the form of its previous editions. We have therefore very little to say of it, otherwise than to endorse the favorable judgment which has demanded ten editions in fifteen years. The present edition has been revised, rearranged, and where necessary rewritten, to keep abreast of the great advances in the science and practice of public health. It therefore still remains a thoughtful and most suggestive guide for the purposes of the medical officer of health and of the student. E. L.

Diseases of the Liver, Gall-bladder, and Bile-ducts. By H. D. Rolleston, A.M., M.D. (Cantab.), F.R.C.P., Physician to St. George's Hospital, London; formerly Examiner in Medicine at the University of Durham, England. Octavo volume of 794 pages, fully illustrated, including seven colored insert plates. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

This voluminous treatise on the diseases of the liver is an excellent work. The author has gathered together all of the literature upon this subject, and has employed it throughout the book in a manner both entertaining and instructive. The major portion of the text, however, is composed of his own opinions, based upon his wide clinical experience in the treatment of these diseases. A large number of clinical cases are quoted, which cannot help but be of great value to practitioners in diagnosing individual cases. Much attention has been paid to the morbid changes underlying each disease, making possible a rational conception of the subject. In addition to the section on the Diseases of the Liver, the diseases of the gall-bladder and bile-ducts are as ably discussed. The illustrations are unusually excellent, showing both the macroscopic and microscopic appearance of the more important pathological changes. This work is most heartily recommended to the profession. J. S. E.

A Text-book of the Practice of Medicine. By James M. Anders, M.D., Ph.D., LL.D., Professor of the Practice of Medicine and Clinical Medicine, Medico-Chirurgical College, Philadelphia. Sixth edition, thoroughly revised. Octavo volume of 1300 pages, fully illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

In this edition, the sixth, while the general plan of classification adopted in the previous editions has been maintained, there have been many new subjects introduced. Among these are Paratyphoid Fever, the Fourth Disease, Trypanosomiasis, Orthostatic Albuminuria, Transcortical Aphasia, Adiposis Dolorosa, and Amaurotic Family Idiocy. It is evident that the author has gone over thoroughly an immense amount of literature to bring the entire work down to date, and has at no time confined himself to individual views for the sake of originality. The work certainly fulfils the requirements of a first-class treatise on medicine and its practical application and cannot help but meet the demands of both students and practitioners. J. S. E.

A Text-book of Clinical Diagnosis. By Laboratory Methods. For the Use of Students, Practitioners, and Laboratory Workers. By L. Napoleon Boston, A.M., M.D., Associate in Medicine and Director of the Clinical Laboratories of the Medico-Chirurgical College, Philadelphia. Octavo volume of 547 pages, with 320 illustrations. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

The author has prepared a volume the arrangement of which makes it easy for busy practitioners to consult. A greater portion of the subject matter has been devoted to the technique of the various methods employed in laboratory examinations, and this is both concise and explicit. The work is not intended as a reference book for advanced laboratory investigations, and therefore only those methods which are easily followed out have been described. The author, however, has shown a tendency to exaggerate the relative importance of tests devised by himself, to the exclusion of well-approved and reliable methods, as shown, for example, by the test for Indican. The paragraphs devoted to "Microscopic Study of Fresh Blood" are apt to mislead beginners to make tentative diagnoses upon very insufficient grounds. Taken as a whole the book is good; the illustrations are instructive and well executed; the space devoted to the clinical significance of the laboratory findings is excellent; the type is clear and of large size, and there is every evidence of careful preparation and production. J. S. E.

Handbook of Anatomy. Being a Complete Compend of Anatomy, including the Anatomy of the Viscera and Numerous Tables, by James K. Young, M.D., Professor of Orthopædic Surgery, Philadelphia Polyclinic; Clinical Professor of Orthopædic Surgery, Woman's Medical College of Pennsylvania; Instructor in Orthopædic Surgery, University of Pennsylvania; Fellow of the College of Physicians of Philadelphia; Fellow of the Philadelphia Academy of Surgery; Fellow of the American Orthopædic Association; Member of the American Medical Association, etc. Second edition, revised and enlarged, with 171 engravings, some in colors. Philadelphia: F. A. Davis Company, 1905.

The second edition of this excellent handbook for students has been enlarged, revised, and a number of new cuts added. The nomenclature has been brought up to date to comply with the changes that have taken place since the first edition appeared. Some such book is necessary to the student who is studying anatomy or dissecting, and we heartily recommend it for these purposes. W. P.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

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Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

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B.J.C.D.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

HAS EXPERIENCE SUSTAINED THE MORE RADICAL OPERATION FOR CANCER OF THE UTERUS?[1]

By John G. Clark, M.D.,

Professor of Gynecology in the University of Pennsylvania; Gynecologist-in-Chief to the University Hospital.

In the first enthusiasm following the inauguration of a new policy or the employment of a novel operation, the inventor's forecast may be too rosy unless he be of unusually judicious temperament, and the final results may fall lamentably short of even his least anticipations.

All who have been actively engaged in gynecological surgery have passed through these stages of hope in the treatment of carcinoma of the uterus, but in the end have been disappointed in the ultimate results; and several prominent gynecologists have fallen into a state of direst pessimism relative to the surgical cure of this disease. While the operative statistics up to this time must dampen the enthusiasm of even the most ardent optimist, on the other hand, they are sufficiently encouraging to cheer even the pessimist if he will only give the study of ultimate results an unprejudiced critical review.

It may be of some interest to the Society for me to give a brief review of my present views relative to the operative treatment of cancer of the uterus, for it was in this hospital that I was granted, through Dr. Kelly's courtesy, an opportunity in 1893 to put into effect a more radical operation for the cure of cancer of the uterus. Up to that time vaginal hysterectomy had been the operation of election, and while the ultimate results from this operation, as shown by a review of forty-eight cases by Dr. Russell, were as good or better than those obtained in other clinics, they were still very discouraging. By contrast the thorough operation, as advocated by Dr. Halstead for the breast, was materially lessening local recurrences and increasing the ratio of ultimate cures. The analogy between the breast with its axillary glands and the uterus with its broad ligament and iliac lymphatics appeared so intimate as to urgently suggest the inauguration of a more radical policy in the latter region, in the hope that a greater percentage of ultimate cures might be effected. While the analogy then appeared self-evident and required no proof, the experience of the last twelve years has tended to disprove rather than to sustain the anticipation for a higher rate of recovery. While my experience with the radical operation has not been so extensive as Wertheim's, of Vienna, it has been sufficient to rob me of the stimulating hope that by carrying out the most radical measures the patient may be offered a greater chance for escape from her direful fate. In my first year's experience in the gynecological dispensary I conceived the greatest horror for this disease, for so large a proportion of cases were inoperable when they first came to the clinic, and in a preponderating majority of operable cases there was such quick recurrence that it seemed to me the most active efforts should be made to circumvent the disease, even when considerably advanced beyond its primary site. Hence the principle of operation was adopted to remove as much local and adjacent tissue with associated glands as was anatomically possible. The principle involved in the more radical operation proposed simultaneously by Ries, Rumpf, and myself was to make as wide an extirpation of the uterus and its broad ligaments as possible, and then carefully dissect out the iliac lymph glands. While it was soon recognized that this operation was most difficult and would be followed by a much greater immediate mortality than the simpler vaginal or abdominal hysterectomy, it was still hoped that the ultimate results would fully justify this procedure. These cases, therefore, have been watched with the most absorbing interest, and the conclusions from my own experience, as well as that of others, have caused me to abandon this theory because the results have not sustained it. Part of this principle, however, I still advocate—viz., that all local tissues as far as possible should be removed, for as my experience seems to demonstrate, and as is further sustained by other statistics, our patients die from local continuance of the growth rather than from widespread glandular metastasis. Therefore the widest local operation without consideration of glandular metastasis is advisable, for if the glands are involved recurrence is well-nigh unavoidable, regardless of the most radical measures. No one man's experience is yet sufficient to settle a single point pertaining to any phase of the cancer question, and therefore the safest conclusion may be reached from a collective statistical study.

A very pertinent query in this study is: Does cancer give early metastasis? In answer we have various and very divergent opinions. Ries, who was the first to advocate a radical operation with a view to the eradication of the pelvic lymph glands, still holds the opinion that metastasis occurs

[1] A paper presented before the Johns Hopkins Medical Society, March, 1905.

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very early, and has consistently advocated the principle of glandular extirpation. Cullen was one of the first investigators to go on record against this theory, for he only found in a small proportion of cases involvement of the pelvic lymph glands.

As the result of his study he made the following statement: "As a matter of fact the glands are not often involved, at any rate only very rarely, before the disease has advanced so far that the case has become inoperable." And further, relative to cancer of the body, he says: "It may be safely said that in nearly all operable cases of adenocarcinoma of the body no glandular involvement has taken place." This view of Cullen fully coincides with that of Winter,[1] who found cancerous glands in only 2 cases in 44 autopsies on patients where the disease was still confined to the uterus.

With the statements of Winter and Cullen before us, the necessity for the radical removal of the glands, especially as this extra step unquestionably prolonged the operation very materially and added greatly to the dangers of shock, sepsis, and renal and ureteral complications, seemed much less urgent. Nevertheless, my own policy until the last four years has been in favor of the radical operation with the extirpation of adjacent glands. Of late, however, as I have frequently stated, I consider the removal of the glands of prognostic rather than of curative value. As in many of the practical fields of surgery, so here the radical operation was more or less extensively employed, and Werder, of Pittsburg, antedated Wertheim in the proposal of a radical operation which possessed advantages over the methods employed by Ries and myself. Notwithstanding Werder's advocacy of the more radical operation, he has recently returned to the use of the actual cautery, performing a high amputation along the lines originally laid down by the late Dr. Byrn, of Brooklyn. His experience, therefore, has not apparently justified the more radical procedure.

The statements of Cullen and Winter were quickly challenged by Peiser, Wertheim, Ries, and others, Wertheim claiming that metastases had been overlooked by these observers because serial sections had not been studied. Thus Peiser, in a considerable number of autopsy cases, found the glands involved in 50 per cent. Wertheim, after perfecting his operation, reported 60 cases in 1901, and as a result of careful serial sections of the glands removed, he found 31.7 per cent. of all cases involved, and in 15 per cent. of the earliest cases there were demonstrable metastases. He therefore discovered a much larger percentage than either Winter or Cullen, and thus justified the further trial of the more radical operation.

Schauta, of Vienna, who has had very extensive experience with vaginal hysterectomy, has recently studied the question of glandular metastases in cancer of the uterus most thoroughly, and has furnished data which strongly sustains his plea for a radical local operation rather than a widespread search for glandular metastasis. He therefore takes strong issue with Wertheim.[1] In this study of 60 cases which have died, either as the result of the operation or from the natural effects of the cancer, each case has been most thoroughly investigated to determine the frequency of glandular metastasis and the relationship of the pelvic to the higher retroperitoneal lymph glands.

In order to study the glandular areas according to topographical localities he divides them as follows: first, the sacral glands, which are found on the anterior surfaces of the sacrum and in the mesorectum; second, the iliac glands, which are situated in the triangle between the external and internal iliac vessels, also along the course of the common iliac vessels. These two groups of glands he looks upon as being the so-called operable areas in that they may be reached during the course of hysterectomy.

Under the first group of glands which cannot be reached by an operation are the glands situated along the sides of the aorta, from its bifurcation upward to the renal vessels; second, the cœliac glands, which are situated between the renal vessels and the diaphragm; third, the superficial inguinal glands; fourth, the deep inguinal glands. While the inguinal glands are unquestionably operable, they are comparatively seldom involved in cancer of the cervix. Therefore they need not be taken seriously into consideration in the more radical methods of operation.

In Schauta's series of 60 cases death followed operation in 11, 9 died of intercurrent affections, and 40 from the natural termination of the disease. In considering the question of operation in these cases from the standpoint of glandular metastasis, Schauta divides them into the following groups: Group 1, both the lower and upper series of glands free of disease in 26 cases, 43.3 per cent.; group 2, the lower pelvic glands carcinomatous, while the upper glands were free in 8 cases, 13.3 per cent.; group 3, the lower glands free, but the upper the seat of metastasis in 5 cases, 8.3 per cent.; group 4, both the upper and the lower series of glands involved in 21 cases, 35 per cent. From this study of cases it is evident that there were 48.5 per cent. of cases in which the lower glands were carcinomatous, but only 13.3 per cent. could have been saved by the most radical operation, for in the larger proportion the upper series of glands which could not be removed were involved.

It is also a rather startling fact that notwithstanding the majority of these patients came to their death as the result

[1] Ueber die Recidive des Uterus Krebses, insbesondere uber Impfrecidive, Zeit. f. Geburt. u. Gynäk., 1893, Bd. xxvii. s. 101.

[1] Die Berechtigung der vaginalen Totalexstirpation bei Gebarmutterkrebs. Monat. f. Geburt. und Gynäk., 1904, Bd. xix. H. 4.

of the natural termination of the disease, 43.3 per cent. were entirely free of carcinomatous metastasis. *In my opinion it is this class of cases with which we must definitely reckon in considering the permanent cures following hysterectomy for cancer.*

Relative to the time of metastasis, recent observers have pointed out the peculiar fact that the extent of the disease by no means furnishes any criterion as to the presence or the extent of the metastasis. Also another fact which has been prominently brought into the foreground, especially by Schauta, Kundradt, and others, is that the size of the gland is of no clinical value in deciding whether it is the seat of cancer. In this series of Schauta's cases it is seen that, notwithstanding the fact that the majority of his patients died without any operative intervention, in almost one-half of the cases the cancer was still a local disease. Certainly as yet no one has satisfactorily explained the peculiarities of metastases in these cases; why a cancer which is only starting upon one lip of the cervix should give metastasis and another case of the most advanced local involvement should be free from this sequel.

Another peculiarity of glandular metastasis is that a lymph gland may be greatly enlarged and can be palpated as a well-defined mass, and yet may not be involved, whereas a minute adjacent gland is found on microscopic examination to be the lodging place for cancer cells. Relative to this question of lymphatic involvement Schauta, Kroenig, and others are skeptical as to whether cancer always continues to develop after it is lodged in the lymph glands. They believe in a certain proportion of cases the malignant cells do not grow, but on the other hand are either retained in the lymph glands as foreign bodies or undergo degeneration and are destroyed.

From these observations it would seem that the prolongation of a radical operation, with its attendant higher mortality, may not be justifiable. This would seem to be especially true if in general Schauta's observations are confirmed, that in only 13.3 per cent. of cases where there is a glandular metastasis it is localized to the pelvic areas, which might be totally extirpated. Then, too, a point which has been prominently considered lately is the fact that the glands alone are not the sole nesting places for cancer cells, for the lymph vessels and connective tissue surrounding these vessels have in some instances been involved.

With these facts before us the outlook for an improvement in the mortality rate following a more radical operation with extirpation of the lymph glands is, to say the least, discouraging. While we may consider Schauta's statistics as coming from an operator who is prejudiced in favor of vaginal hysterectomy, we do not find much to offset his conclusions in the work of Wertheim and his assistant Kundradt, who are equally strong in favor of the radical operation. As the results of Schauta's study he comes to the following conclusions: first, in any case of uterine cancer, in which the operable group of glands is involved, it is probable that the higher situated glands are likewise invaded, thus making a radical operation impossible; second, large, hard, infiltrated glands are frequently not cancerous; third, even the smallest glands may be cancerous; fourth, cancer is not strictly confined to the glands, but may be found in lymph spaces, connective tissue, or in veins between the glands.

In Wertheim's last report of cases I am inclined to feel that he has not sustained his position; on the contrary, I believe his statistics have sustained his opponents' contention.

In Kundradt's study of 80 operative cases of Wertheim's he found the location of the cancer as follows:

	CASES.
A. Cervix involved, both parametria free, lymph glands of both sides free	32
B. Cervix involved, one parametrium involved, lymph glands of both sides free	15
C. Cervix involved, both parametria involved, lymph glands of both sides free	7
D. Cervix involved, one parametrium involved, lymph glands of the same side involved	7
E. Cervix involved, one parametrium involved, lymph glands of the opposite side involved	3
F. Cervix involved, both parametria involved, lymph glands of one side involved	7
G. Cervix involved, one parametrium involved, lymph glands of both sides involved	1
H. Cervix involved, both parametria involved, lymph glands of both sides involved	4
I. Cervix involved, parametria free, lymph glands of one side involved	4

From this analysis of Wertheim's cases it will be seen that in 54 the lymph glands were not involved, and therefore the radical operation at least could not be said to have helped the prospects of permanent cure, while the same procedure certainly was attended with much greater dangers of immediate mortality. If to the remaining 26 cases we were to apply the results of Schauta's research, only 13 per cent. were operable from the radical standpoint, for if his observations are correct in only this small percentage was the metastasis located solely in the pelvic glands removed by the radical operation.

In considering how cancer of the cervix grows, Kundradt divides the cases into three groups:

1. Cancer grows in a compact mass spreading uniformly out into the parametrium, and involving the latter in such a way that the advancing growth is not sharply circumscribed. In a second class of this group the carcinoma is well circumscribed to the cervix, but in one place there is an outgrowth into the parametrium, usually along a lymph channel around the bloodvessels, occasionally along the nerve sheaths.

2. Cancer sharply circumscribed to cervix, but out in the parametrium metastases, either in the lymph nodes or in the lymph vessels.

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3. Cases in which both groups are combined, the primary tumor either growing in continuo from the cervix into the parametrium and further out in the parametrium metastasis, or the cancer grows in continuo on one side, while the metastasis is on the opposite side.

That Wertheim is laying less stress upon the extirpation of the gland is, I believe, shown in two paragraphs in his report of 1901. He says:

First, it is an error to consider that the chief stress is laid upon the extirpation of the glands. Just as important, indeed more important, is the widest possible removal of the parametrium. Second, according to his latest observation it is not necessary to remove the glands if they are not enlarged.

Contrary to Wertheim's conclusions upon the last point, Oehlecker, von Rosthorn, Kroemer, Cullen, Sampson, and others claim that the size of the gland bears no relationship to metastasis, for large beaded glands may contain no trace of cancer cells, whereas in the immediate vicinity a very small gland may contain many epithelial cells. Thus Wertheim's latest statement, that unless the glands are palpably enlarged they need not be extirpated, is based upon a fallacy and cannot be maintained, for if, as now appears certain, the foregoing observers are correct, the entire force of Wertheim's argument in favor of the removal of the glands falls to the ground, and if he follows out the last principle we will never be able to determine how much the removal of the glands has influenced the permanent recoveries. Certainly a considerable number of cases in which no palpable glands are found will still be the seat of more or less metastasis. If therefore the principle of glandular extirpation is to be of avail, it must be systematically carried out in all cases, whether the glands are palpable or not. As I view this question I believe that Wertheim's cases sustain rather than disprove Schauta's argument. From the study of Wertheim's operative cases we find that in 59 per cent. the lymph glands were not involved. In Schauta's series, largely of cases dying from the natural results of the disease, 43.3 per cent. were free of glandular metastasis.

When we take into consideration the fact that there is no regularity of metastatic distribution, that the earliest cases may have already given metastasis, that when the lower accessible glands are involved, the upper inaccessible glands, with the exception of only 13 per cent., are also involved, little argument is left in favor of the extensive dissection of the glands with the largely added mortality that must necessarily follow this step from shock, infection, and other complications. My own conclusion, therefore, although very reluctantly reached, for I had hoped for radical improvements in permanent results, is that we lose more than we gain in the radical operation when the glands are painstakingly extirpated, and to remove here and there a palpably enlarged gland will certainly not promote the patient's interests so far as a radical cure is concerned. My own rule, therefore, is to remove one or more glands for microscopic examination, provided they are palpably enlarged and easily accessible. If we are not to look for improvement in ultimate results from the radical operation with the removal of the glands, from what operative procedure may we gain the greatest good? Shall it be a high amputation of the cervix, either with the knife or actual cautery, a simple vaginal hysterectomy, a Schuckart's vaginal hysterectomy, facilitated by a paravaginal incision, or a radical operation of Wertheim's? Of these various methods I still adhere to the abdominal. This is carried out most radically with the actual cautery, so far as the vagina and parametrium are concerned, and in this we revert to the principle so strongly insisted upon by Russell after his study of 48 vaginal hysterectomies in the Johns Hopkins Hospital. He found almost invariably that there were recurrences at the site of the vaginal scar, and not in more or less widely remote metastatic areas. The rule, therefore, to which I adhere is to remove all possible tissue in the vicinity of the primary site of the growth, using the cautery rather than the knife. In general the principles laid down in Wertheim's latest publication are followed, stopping short, however, with the removal of a considerable cuff of vagina with the uterus, and as much parametrium as is possible, and not prolonging the operation by a search for glands. In acting upon this principle I am influenced by the fact that as yet no operation has saved 50 per cent. of cases, and that in Wertheim's operable cases 59 per cent. showed no glandular metastasis, while even in the far advanced cases of Schauta there were 43 per cent. free of lymphatic involvement, and that of the remainder which were involved only 13 per cent. could have had their chances of a more radical cure enhanced by removal of the glands.

This small percentage of possibility is at least equalized or more than offset by the much greater immediate mortality of the very radical operation.

A CLINICAL STUDY OF THE COMPLICATIONS ARISING IN SIXTY-THREE CONSECUTIVE CASES OF OVARIAN TUMORS, WITH SPECIAL REFERENCE TO MALIGNANCY.[1]

By C. C. Norris, M.D.,
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It is the intention in this paper to take up the complications occurring in sixty-three consecutive cases of ovarian tumors. Simple retention cysts, even when of moderate size, are not included in this list. Malignancy being by far the most frequent and important complication, if complication it may be called, will be taken up first.

Malignant growths of the ovaries may occur in two ways: either the ovary may be primarily attacked by a malignant growth, the organ previously having been healthy; or a hitherto benign ovarian cyst, which has been present for years, may become the seat of a carcinomatous change. No reference will be made in this paper to metastatic new-growths of the ovary. There will undoubtedly be many cases of malignant disease of ovaries which will not come under observation until so far advanced that it will be impossible to state definitely the original condition of the ovary at the time of the beginning of the malignant process. In a general way, however, it may be stated that those cases in which the specimen is very hard and indurated are more apt to have been primarily a malignant process; while those specimens which are very cystic with comparatively thin walls are more likely to have originated as a benign cyst. The history of the cases will often aid in deciding this point, as in Case VI. the patient had been suffering from the symptoms of a cyst, mainly pressure symptoms, for nearly ten years; it is certain that if this case had originated as a malignant growth the patient would have succumbed before the expiration of this length of time; and lastly, a careful microscopic examination will frequently reveal the type of the original growth. The prognosis is probably rather more favorable in those cases in which carcinomatous degeneration occurs on an originally benign ovarian cyst than where the disease is primarily malignant.

The frequency with which malignant diseases of the ovaries occurs varies considerably with different operators, as a glance at the following table will show:

Olshausen finds	15	per cent.	of all ovarian tumors	malignant			
Schroeder	" 16	"	"	"	"	"	
Fritsch	" 18	"	"	"	"	"	
Leopold	" 23	"	"	"	"	"	
Kelly	" 8	"	"	"	"	"	
Freund	" 20	"	"	"	"	"	
Werder	" 25.3	"	"	"	"	"	

[1] This article will also appear in the January number of the American Journal of Obstetrics.

By adding seven exploratory laparotomies performed for this condition, 20.4 per cent. is reached in Werder's series. This, he says, does not represent the full percentage, as there were many inoperable cases.

In a series of sixty-three cases of ovarian tumors operated on in the Gynecological Department of the University Hospital since 1899 there have been ten cases of malignant disease of the ovaries, giving a percentage a little over 15.8 per cent. This, as in Werder's series, does not represent the full percentage of malignancy, as there were several inoperable cases.

In our laboratory the classification suggested by Orthman has been adopted and will be followed in speaking of the different varieties of ovarian tumors.

Although parovarian cysts are not true ovarian cysts, still as their clinical symptoms closely simulate those of ovarian cysts, and the complications are practically the same, it has been deemed best to include them in this series.

Case I. *Pathological No.* 302.—Aged fifty years; adenocarcinoma glandulare cysticum ovarii, right side; cystadenoma ovarii; pseudoglandulare, left side. Macroscopically and clinically this case appears to be one of bilateral multilocular ovarian cysts. Both cysts were moderately large and presented no gross evidence of malignancy. On histological examination, however, the cyst which sprang from the right ovary was found to have undergone carcinomatous degeneration. The patient had no symptoms until seven months before operation. The operation performed was bilateral salpingo-oophorocystectomy. There were no metastases at operation. The patient made a normal convalescence.

Case II. *Pathological No.* 493.—Aged sixty years; adenocarcinoma glandulare cysticum ovarii. The specimen represents two ovarian tumors; they are of moderate size and similar in general characteristics; for the main part they are cystic, but many areas of almost stony induration are found throughout their substance. The first symptoms this patient noticed were seven months before the operation. The operation performed was a panhysterectomy, bilateral salpingo-oophorocystectomy. There were no metastases present at operation. This patient suffered from an aortic lesion so severe that the medical men who were asked to examine her advised that no operation be performed unless it was a matter of life and death for the patient. Ether was used. She stood the anaesthesia well, and at the time of her leaving

the hospital her heart symptoms were greatly improved. Convalescence was normal.

Case III. *Pathological No.* 608.—Aged forty-six years; adenocarcinoma glandulare cysticum ovarii. The specimen consists of two ovarian tumors. They are moderate-sized, one slightly larger than the other, the greatest diameter of the larger being 31 cm. They have the usual appearance of multilocular ovarian cysts which have undergone chronic inflammatory changes. On section it is found that they are mainly cystic; there are many hard, indurated areas found throughout their substance. The first symptoms noticed by the patient were about six months before the operation. The operation performed was a panhysterectomy, bilateral salpingo-oophorocystectomy. There were no metastases noticed at operation. The patient was septic and in a very bad physical condition at the time of the operation. She died from peritonitis thirty-six hours after the operation.

Case IV. *Pathological No.* 666.—Aged forty-five years; adenocarcinoma glandulare cysticum ovarii. Specimen consists of an ovarian tumor, cystic in character, spherical in shape, its greatest diameter being 24 cm. The surface shows numerous tags of adhesions. On section the tumor presents the usual appearance of a multilocular ovarian cyst. The first symptoms referable to this tumor were noticed by the patient four months before operation. Operations performed were: right salpingo-oophorocystectomy, appendectomy, radical cure of bilateral inguinal hernia, and myomectomy for a small subperitoneal fibroid. The patient had a normal convalescence.

Case V. *Pathological* No. 753.—Aged fifty-five years; adenocarcinoma glandulare cysticum ovarii. Specimen consists of an ovarian tumor undergoing necrosis, due to torsion; greatest diameter of tumor 32 cm. The tumor is partially collapsed, multilocular, infiltrated with blood, and shows numerous adhesions. The uterus accompanying the specimen is somewhat enlarged, and on section shows a new-growth at the fundus. The first symptoms noticed by the patient were seven months ago. The operation performed was a panhysterectomy, bilateral salpingo-oophorocystectomy. This case showed metastases to the uterine body and clinically simulated a suppurating uterine fibroid. Normal convalescence.

Case VI. *Pathological No.* 754.—Aged sixty-eight years; adenocarcinoma glandulare cysticum ovarii. Specimen consists of a large ovarian cyst undergoing gangrene; greatest diameter of cyst about 35 cm. The uterus accompanying this specimen is enlarged and contains a number of intramural and subperitoneal fibroid tumors. The first symptoms noticed by this patient occurred ten years ago, when the abdomen began to enlarge, and since then has been steadily increasing in size. For the last few days prior to operation the patient has had severe pain over the abdomen and especially in the hepatic region. At operation this latter pain was found to be due to adhesions to the gall-bladder and liver.

Operation: supravaginal hysteromyomectomy, bilateral salpingo-oophorectomy.

This patient had a normal convalescence, and on leaving the hospital appeared well except for occasional attacks of indigestion. The after-history of this case is that she was nearly well for a year and then began to have persistent diarrhœa, and, regardless of everything that was done, this continued until her death, about sixteen months after the operation. The probabilities are that this was due to a recurrence of the carcinoma.

Case VII. *Pathological No.* 774. Aged fifty-six years; adenocarcinoma glandulare cysticum ovarii. The specimen consists of a small piece of cyst wall excised at operation for diagnostic purposes. The clinical diagnosis before the operation in this case was large ovarian cyst; ascites, consisting of thick fluid. At operation the case was found to be inoperable on account of the extremely bad physical condition of the patient while on the operating table; at this time a large amount, fully two gallons, of thick, blood-tinged, colloid material was removed. The cyst was densely adherent to the surrounding structures. The patient had a somewhat prolonged convalescence, but finally left the hospital in good condition. About one year after the first operation the patient again presented herself at the hospital, suffering from a recurrence of the previous disturbance. During these twelve months the patient had improved in many ways. It should be stated that the small piece of tissue removed at the first operation showed no evidence of malignancy on careful histological examination. A second operation was performed, and the tumor proved unquestionably to be malignant. In view of this fact and the impossibility of entirely removing this growth, which originally sprang from the right ovary, a radical operation was not performed. The convalescence from the second operation was normal. Following convalescence the patient complained of considerable pain through the abdomen, most marked in the lower right quadrant. The *x*-ray was used and dispelled the pain at once.

Case VIII. *Pathological No.* 924.—Aged twenty-two years; adenocarcinoma glandulare cysticum ovarii. Specimen consists of two medium-sized ovarian tumors similar in general characteristics and presenting the usual appearance of cystic carcinoma of the ovaries. The patient noticed the first symptoms eight months before operation. Operation consisted in a bilateral salpingo-oophorocystectomy for palliative results only, as it was found that there were numerous metastases, one of which involved the sigmoid flexure near its distal extremity. On account of this, and as the intestine was

almost entirely constricted, an artificial anus was made in the inguinal region. The patient recovered from the operation and at the end of six weeks was transferred to another hospital.

Case IX. *Pathological No.* 926.—Aged forty-three years; adenocarcinoma papillare ovarii; bilateral. The specimen consists of two similar, medium-sized ovarian tumors, papillomatous in character. First symptoms occurred seven months prior to operation. Supravaginal hysterectomy, bilateral salpingo-oophorocystectomy was performed. There were no metastases present at operation. The patient had normal convalescence.

Case X. *Pathological No.* 987.—Aged thirty years; adenocarcinoma; glandulare cysticum ovarii. Specimen consists of a medium-sized multilocular ovarian cyst, apparently undergoing suppuration. There is one area about 5 cm. in diameter and a few smaller ones which show marked hardness and induration. Right salpingo-oophorocystectomy. There were no metastases present at operation. This is undoubtedly a case of carcinomatous degeneration of an originally benign ovarian cyst, as the patient has had pressure symptoms and menstrual disturbances for over three years, but for the last four months has been losing weight and strength and has had considerable pain, which prior to this time was not a marked feature, and was of a different character. The thought of malignant disease of the ovary occurred before operation, but after examining the gross specimen it was decided that the cyst was probably a multilocular ovarian cyst undergoing suppuration. The malignant process was only discovered by the microscope after sections from nine different parts of the tumor had been examined. Some of these sections showed no evidence of malignancy. The patient made an uncomplicated recovery. Examination of this patient four months after the operation showed no evidence of recurrence. Patient had gained in strength and weight and felt well. Death occurred fourteen months after operation from recurrence.

Case XI. *Pathological No.* 168.—Adenocarcinoma glandulare ovarii. Specimen consists of a small ovarian cyst, its greatest diameter being about 12 cm.; it is multilocular; its surface shows many adhesions; throughout its substance are many hard indurated areas. In this case there were metastases to the iliac glands.

Case XII. *Pathological No.* 178.—Adenocarcinoma glandulare ovarii. Specimen represents a large ovarian cyst, its greatest diameter being about 34 cm. It presents the usual appearance of a multilocular ovarian cyst.

Case XIII. *Pathological No.* 187. Adenocarcinoma glandulare cysticum ovarii. Specimen represents a moderate-sized ovarian cyst. For the main part the surface of the specimen is smooth, although a few adhesions are seen on its posterior surface. The walls are moderately thin; there are two or three hard indurated areas; histologically these areas show carcinomatous change.

Case XIV. *Pathological No.* 185.—Adenocarcinoma glandulare cysticum ovarii. Specimen represents a moderate-sized ovarian cyst, similar in general character to the case represented by Pathological No. 187; but this case shows more numerous and larger areas of hardness.

Case XV. *Pathological No.* 186.—Adenocarcinoma glandulare cysticum ovarii. Specimen represents a rather small ovarian tumor, for the most part hard to the touch, although a few cystic areas are present.

The last five cases are museum specimens only. The clinical history being unknown, they are added to this list to show how difficult and in many cases impossible it is to detect a malignant process in an ovarian cyst from the gross appearance of the specimen. These cases are, of course, not included in the sixty-three cases of ovarian cyst from which the statistics in this paper have been drawn.

All the specimens from the above cases were subjected to a rigid microscopic examination, the routine calling for at least two blocks from each tumor, and in some cases ten or twelve were taken; the advantage of this routine being shown in the fact that in a large number of these cases a positive diagnosis could not have been given without the aid of the microscope, and in one or two cases malignancy was not even suspected until a histological diagnosis had been made.

Of these 15 cases, 6 were bilateral, 4 were bilateral carcinoma, while 2 showed a benign multilocular cyst on one side and carcinoma on the other; of the 9 remaining, 5 originated in the right ovary and 4 from the left side. In this series there were 3 large cysts, 10 medium-sized, and the remainder small. The question as to how many of these 10 cases were originally benign and how many were originally malignant it is impossible to answer positively; but upon careful study of the histories and of the specimens it would appear that 4 cases were originally malignant, that 4 were carcinomatous degeneration of an originally benign ovarian cyst, and in the 2 remaining cases the type of the original growth is in doubt. The age of the 10 patients varied from twenty-two to sixty-eight years, the average being a little over forty-six and a half years. Two of the patients were under thirty years of age, showing that this condition not infrequently occurs in young women.

Two of these 10 cases showed metastases at operation, one to the body of the uterus and one to the mesenteric glands and intestine; in the latter the tumor was densely adherent to the intestines and mesentery.

In this series there was an operative mortality of 10 per cent, the one death occurring (Case III.) in a case that was already septic before operation, and in which the general condition of the patient was extremely bad. This patient

died from peritonitis at the end of thirty-six hours. In Case VIII., in which an inguinal colostomy was performed, the patient was transferred to another hospital six weeks after the operation. The remaining 8 cases left the hospital in good condition. The operative mortality in any large series of cases will probably be considerably larger than ours, 10 per cent., as is shown by the following statistics:

Cohn reports 100 cases of malignant disease of the ovaries operated on in Schroeder's clinic; there was an operative mortality of 20 per cent.; 15 per cent. soon succumbed after operation to disease, but 10.5 per cent. were living at the end of one year. In 5 per cent. the cure was maintained at the end of three to five years. Fritsch and Leopold soon followed with as good reports. Kratzenstein gives the results of 100 cases treated at the Universitäts-Frauen-Klinik in Berlin between 1879–92, in which a subsequent course is known. In this series the operative mortality was 28 per cent.; of the remaining 72, 36 died from recurrence and 36 were permanently cured. In Werder's excellent paper, upon malignant disease of the ovary, he reports 20 cases subject to radical operation; there was a mortality of 15 per cent., 7 of these deaths were due to recurrence and 1 was in doubt. In our series of 10 cases, which are the entire number of this condition occurring in 1588 consecutive gynecological cases, there were no cases of sarcoma of the ovary, showing that this disease is a comparatively rare one. L. Pick, in 1894, collected 23 such cases; 12 of these were round-celled sarcoma; 10 of the 23 were under twenty years of age, and 6 of these were round-celled sarcoma; 9 of the 23 were bilateral affections, and 6 of the 9 were round-celled sarcoma. One of his own cases had had constant symptoms for a year and a half, but at operation there were no metastases; this was a case of round-celled sarcoma; and Pick, as a result of his study of these 23 cases, draws the conclusion that the disease frequently occurs in young women, and that metastasis often does not take place until late.

In a recent article Pick has changed his views in regard to the classification of some of these tumors; he has come to the conclusion that one of these tumors is not a true sarcoma, but is a teratoma; he has positively identified certain cells as Langhans' cells, syncitium, and trophoblasts. The examination shows the tumor to be a teratoma with endodermal (glands lined with goblet cells), mesodermal (sarcomatous connective tissue), and ectodermal (central nervous system and chorioepithelial tissue) constituents. Pick has given the name epithelioma chorioectodermale to this variety of tumor. Landau reports five such tumors; all of these occurred in young girls. The tumors are clinically very malignant. All the patients have died but one, who was alive nine months after the operation. Three patients had metastases to the lungs. These tumors, epithelioma chorioectodermale, may be regarded as a teratoma in which there are epithelial elements which have developed to the exclusion of the other kinds of tissue found therein. In their metastases they resemble chorioepithelioma rather than carcinoma, in that they are distributed through the bloodvessels and not through the lymphatics. All the tumors reported by Landau were unilateral; three of the tumors were solid and two more or less cystic. The largest tumor was the size of an adult head; all the tumors were rounded and showed lobulation on their surface. Concerning the frequency of this growth Landau mentions twenty-eight solid ovarian tumors removed in his clinics which have been subjected to careful histological examination; fifteen of these were fibrosarcoma or spindle-celled sarcoma; one was a mixed sarcoma; two were small round-celled sarcoma; four were endotheliomata, in the sense of Marchand and Pick. Five or perhaps six belong to the epitheliomata chorioectodermales, or about 15 per cent. of growths hitherto called "alveolar sarcoma with carcinomatous-like structure" or "endothelial tumor rich in glycogen," are really of this newly described type. Schmaus reports a tumor which from his clinical and histological description closely resembles this newly described variety, but he believes it to have been a peculiar transformation of an ordinary carcinoma.

Ohl, Cohn, Olshausen, Pick, and Kratzenstein agree that the prognosis for ultimate cure of cases of sarcoma of the ovary is very much more favorable than is the prognosis in cases of carcinoma of the same organ. Pfannenstiel in a recent article says that he believes there are about 30 per cent. of permanent cures resulting from operation on cases of sarcoma of the ovaries. He further says that the fibrosarcoma is quite benign; next comes the spindle-celled, but that the soft, round-celled sarcoma are very malignant.

In taking up the subject of the papilloma of the ovaries, or what Kelly terms the clinically "semimalignant tumors of the ovaries," it is found that there are 13 cases of this condition in the 63 cases of ovarian tumors from which the statistics for this paper were derived. Of these 13 cases only 1 has been histologically or clinically malignant; this is Case IX. Regarding the frequency with which adenocarcinoma is associated with papilloma there is much difference of opinion, some authors claiming that 50 per cent. of all papilloma are malignant, while others hold that it is a very much smaller proportion. Kelly found the condition present in 2 out of 27 cases which practically conforms to the percentage found in this series. Pfannenstiel found 20 cases of adenocarcinomatous papilloma of the ovary in 43 cases. The fact that benign papilloma of the ovary frequently presents the gross appearance of adenocarcinomatous papilloma should not be lost sight of in operating for this condition, and all efforts should be made to remove the growth even if it is thought to be malignant. It is necessary to make a careful distinction between general carcinomatoses of the

peritoneum, which take place through the bloodvessels and lymphatics, and "contact growths" which result from direct implantation upon the peritoneum, this latter process frequently being benign, and, as Pozzi has pointed out, may be compared in many cases to papilloma and warts of the skin. This important distinction was long ago pointed out by Freund, but is at present too frequently disregarded.

In examining the reports of any series of operation for papilloma of the ovaries it will be found that there are many cases in which the primary growth is removed, but contact growths on the peritoneum have been left, and that these cases have recovered and had no recurrences.

Regarding the advisability of operating on all cases of malignant disease of the ovaries in which the entire new growth can be removed there is no difference of opinion; but the question of operating upon the so-called "border-line cases," in which it is doubtful if the entire growth can be removed, there is great diversity of opinion. These "border-line cases" when of carcinomatous origin almost certainly die either from the direct effects of the operation, these cases seeming to be peculiarly susceptible to infection, probably because in the majority of these cases there has been a moderate or long-standing ascites and the absorbing properties of the peritoneum have been much reduced, or more frequently they die from a recurrence of the original growth. On the other hand, those cases of papillomatous origin usually recover. The fact that the diagnosis between these two conditions before operating is frequently not possible should lead the surgeon to operate on these cases and give the patient every possible chance. It should also be remembered that in those cases which have originally been benign tumors, but which have become malignant, the malignant process at the beginning is very limited and may be entirely removed, while it may be impossible to remove the entire original growth. Even in cases supposed to be totally inoperable, from the standpoint of removing the entire growth, it is doubtful if operations should not be performed; for diagnostic purposes and because operations will not infrequently give a very marked temporary relief from symptoms, as in Case VII., where an exploratory laparotomy was performed and ascites removed, the operation gave the patient nearly one year of relief from hitherto painful symptoms; also in Case VI., the patient was nearly well for one year.

In quite a large proportion of cases of benign papilloma of the ovaries in this series it was impossible to give a positive diagnosis until the specimen had been subjected to a microscopic examination; for this reason also the patient should be given the benefit of the doubt.

The complications which may occur in any given case of ovarian tumor are very numerous. It would be impossible and tiresome in a paper of this character to give an individual history of each complicated case, but an endeavor will be made to give a general description as to the size, adhesions, and other causative factors occurring in each complicated case. The number of each variety of ovarian cyst, classified according to Orthman, is as follows:

19 parovarian cysts.
5 teratoma cysticum ovarii.
1 teratoma solida ovarii.
3 cystadenoma ovarii serosum papillari petrificans.
10 cystadenoma ovarii pseudomucin papillare.
15 cystadenoma ovarii pseudomucin glandulare.
1 adenocarcinoma papillare ovarii.
10 adenocarcinoma glandulare cysticum ovarii.

Or under a broad clinical classification there are:

19 parovarian cysts.
6 dermoids.
13 papilloma.
15 multilocular ovarian cysts.
10 adenocarcinoma, either primarily carcinoma or a carcinomatous degeneration.

In examining this series of cases it is found that the three most important complications occurring in it, with the exception of malignancy, are torsion, rupture, and suppuration.

Torsion may occur in two ways, either a sudden twist of the pedicle practically cutting off the entire blood supply, causing intense symptoms of shock, soon followed, unless operative interference is at once instigated, by peritonitis and death; or what is more common, a twist of the pedicle may occur not entirely shutting off the blood supply, but pathologically causing marked engorgement of the cyst, because of the veins having thinner walls than the arteries and are therefore more easily shut off, and clinically causing the symptoms of more or less marked peritonitis. It should be borne in mind in regard to the peritonitis resulting from rupture or torsion of an ovarian cyst that it is a mechanical peritonitis and not bactericidal; at all events this is usually the case in its early stages. This fact has been pointed out by Beyea.

Munde has drawn attention to the fact that large ovarian cysts usually have thick broad pedicles and that the cysts more or less entirely fill the pelvic and abdominal cavities, and therefore are less liable to torsion than small cysts.

The cases in which torsion is most likely to occur are those in which the cyst is small, in which the pedicle is long and thin, and in which the abdominal walls are relaxed. The irregular-shaped tumor, such as is frequently seen in multilocular ovarian cysts, is also probably a causative factor, especially as the tumor grows and is forced out of the pelvis past the promontory of the sacrum, it can easily be imagined how an irregularity in its outline may cause it to twist. It is believed by some that the peristaltic movements of the intestines and their frequent distention in conjunction with small tumors, which have long pedicles, allowing them to

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rise out of the true pelvis, play an important part in the causing of torsion. The gradual growth of a uterine fibroid or of a pregnant uterus, or the sudden emptying of the latter, are also causes. Munde reports a case in which he caused torsion by a bimanual examination. Accidental jars or shocks or the lateral recumbent position may also cause this condition. In one of the cases to be reported in this paper the patient was awakened from sleep by a sharp abdominal pain, which was soon followed by other symptoms of torsion; at operation the diagnosis was confirmed. The woman had felt perfectly well before going to sleep. Untwisting of a pedicle may occur from the same causes which brought on the original torsion, but it is hardly necessary to say that such a condition is so rare that it should not be considered in the treatment of a case.

The most frequent form for torsion to assume is for one twist to occur at a time and for each twist to cause an attack of peritonitis. Without a pelvic or abdominal examination, the symptoms arising from these attacks are not unlike an acute attack of appendicitis, but in this latter condition the pain is more frequent, or at all events in the beginning, situated over McBurney's point, while in a cyst it may originate in any part of the lower abdomen. The diagnosis should usually be easy. Munde gives the following excellent clinical description of torsion:

"A moderate distention of the subumbilical region, with greater prominence either in the median line or on either side; rapid formation of the swelling, which, perhaps, was merely noticeable before; more or less tenderness on pressure; tense but distinct fluctuation with single or interrupted wave, according as the cyst is single or multilocular; outlines of swelling generally distinct, but sometimes diffused; dulness on percussion over area of swelling; tumor palpable through anterior vaginal vault and continuous with suprapelvic swelling; uterus generally posterior to vaginal swelling; fluctuation wave in vagina continuous with abdominal wave; temperature somewhat elevated, perhaps 102°; pulse rapid and small; general depression; anxious countenance. The attack has usually come on suddenly and may have been preceded at an interval of several weeks or months by a similar or less marked seizure, attended by severe pain."

It is not uncommon in cases in which torsion has occurred to find the cyst occupying the opposite side of the abdomen, from which it originally sprang. Torsion should always be borne in mind in cases of sudden abdominal pain occurring in women known to be suffering from an ovarian tumor. Torsion occurs in about 24 per cent. of all cases of dermoid cyst of the ovary. Olshausen many years ago pointed out its frequency in this condition. In the series of 63 ovarian tumors reported in this paper, torsion occurred ten times, or in nearly 16 per cent. of all cases, occurring in the different variety of cysts, as follows:

Five times in 15 cystadenoma ovarii pseudomucin glandulare.

Twice in 9 cases of cystadenoma serosum glandulare.

Once in 2 cases of cystadenoma ovarii serosum papillare petrificans.

Once in 5 cases of teratoma cysticum ovarii.

Once in 10 cases of adenocarcinoma glandulare cysticum ovarii. Or according to the clinical classification torsion occurred:

Seven times in 15 cases of multilocular ovarian cyst.

Once in 6 dermoid cysts of the ovary.

Once in 10 adenocarcinomatous cysts of the ovary.

Once in 13 papillomatous cysts of the ovary

Four of these 10 cases in which torsion occurred were large cysts; 5 were medium-sized, and but 1 was small. This proportion is rather unusual, as has already been stated; torsion is usually supposed to be more common in small cysts. A large cyst in this series is one which has for its greatest diameter a measurement of 35 cm. or more; a medium-sized cyst is between 20 and 35 cm., and a small cyst below 20 cm. It is worthy of note that in 19 cases of parovarian cyst there was none with twisted pedicle, in fact none of the parovarian cysts showed any serious complications. In 10 cases of adenocarcinoma there was but 1 case showing twists in the pedicle; this may, in part, be accounted for by the fact that the malignant tumors of the ovary are much more frequently adherent to the pelvis, and in this way may be prevented from twisting to some extent. But 1 of these 10 cases of torsion was bilateral, and in this the twist occurred on one side only, bearing out the belief that on account of the limited space bilateral cysts are less liable to torsion than single ones. Seven of these cases of torsion occurred in the multilocular ovarian cyst, giving a proportion of nearly 50 per cent. in this variety of tumor. Three of the 10 cases showed rupture at operation, 9 of the 10 cases showed more or less marked peritonitis; 3 of the 10 cases were in extremely bad condition at operation, having high temperature, rapid pulse, and extreme general weakness, requiring most active stimulation at and following operation. In one of these patients the entire operation was performed under local anæsthesia, the patient's condition being such that general anæsthesia would probably have proved fatal. In another of these cases the operation was almost entirely performed under local anæsthesia, ether being given during the last few minutes of operation.

Despite the bad general condition of these patients, and the fact that nine of them were suffering from peritonitis, there was no operative mortality, all the patients leaving the hospital in good condition. This fact seems to the author to strongly bear out the assumption that the peritonitis produced by torsion is mechanical and not bactericidal, at all events in its early stages.

Among the 63 cases of cysts comprising this series there was but 1 case of rupture uncomplicated by torsion. This case, apart from the rupture, presents some very interesting features. Three years before the rupture occurred the patient was operated on at the University Hospital for what proved to be a right-sided multilocular ovarian cyst (cystadenoma ovarii pseudomucin glandulare) of medium size. At this time the left ovary was examined and appeared entirely normal. Convalescence was uncomplicated. Three years after the first operation she was brought to the hospital, with all the symptoms of a ruptured ovarian cyst of medium size; this diagnosis was confirmed at operation, the cyst having sprung from the left side. The specimen appeared to be a collapsed multilocular ovarian cyst containing pseudomucin. Malignancy was strongly suspected on account of the history and appearance, but, although numerous sections were taken from the specimen for histological examination, no malignant process was found, the cyst proving to be of the cystadenoma ovarii pseudomucin papillare teratomatous variety. At the time of this patient's second operation her general condition was very poor and the abdomen was filled with pesudomucinous material. There was no evidence of torsion at operation. The symptoms had come on suddenly after lifting a heavy weight. This case shows how quickly even a benign ovarian cyst may develop and grow, the ovary from which this cyst sprang having been apparently normal three years before.

In this series of cases there is but one case of suppuration of an ovarian cyst uncomplicated by torsion. This occurred in a woman aged fifty-five years, the cyst being moderate in size. She was brought to the hospital in an acute septic condition; there were high temperature, rapid, feeble pulse, and all the symptoms of acute peritonitis. The diagnosis was made of a suppurating ovarian cyst; at operation this was confirmed; the abdomen was filled with foul pus, the cyst on histological examination proved to be of the cystadenoma ovarii serosum glandulare variety. There was no torsion; symptoms had come on rather suddenly three days prior to operation. Death resulted from peritonitis on the third day following the operation. Whether this case was one of rupture, followed by suppuration, it is impossible to state definitely, but from a careful examination of the specimen, both in its gross state and from histological preparation made from it, it seems to be one of suppuration, probably resulting from poor blood supply of the tumor.

In the 63 cases there were 41 cases which showed more or less marked adhesions; in 16 of these 41 cases the adhesions were so dense as to seriously complicate the operation. The 41 cases of adhesions probably do not represent by any means the entire number in which adhesions were present, as in many of the case histories no reference is made to this condition.

Ascites occurred in this series in 53 cases (the 10 malignant cases being excluded) twice, both times with large cysts and both times with cysts of the multilocular ovarian variety (cystadenoma ovarii pseudomucin glandulare). Hemorrhage occurred in the entire series of 63 cases twice; this does not include small hemorrhages occurring into one or two loculations of a multilocular ovarian cyst.

Hydroureter, as a result of pressure, occurred twice, in one case being bilateral, and in the other unilateral.

Exclusive of the complications which were directly caused by the tumor there were 27 other complicated cases, these complications occurring independently of the tumor, such as pregnancy, fibroid tumors of the uterus, inflammatory disease of the tubes and ovaries, endometritis, appendicitis, movable kidney, etc. Whether many of the inflammatory conditions were actually or indirectly the result of the ovarian tumor it is impossible to state, but it would seem that in a certain proportion at least that this was the case. Among the more rare complications which have been mentioned by other authors in regard to this subject and not found in this series, and which may be regarded more as surgical or pathological curiosities, are fusion of two originally separate ovarian cysts and entire calcification or ossification of the tumor. Of course, a moderate degree of calcification is very common and occurred in quite a large percentage of cases in this series. Bolt has called attention to cardiac neurosis in connection with ovarian tumors and believes that this is not an infrequent condition; his studies cover 2000 cases. This condition was not noticed in any of our cases. Bennet in 1848 reported a case of cure of an ovarian cyst by means of an ulcerative opening of the cyst into the bladder; also numerous cases have been reported cured by absorption; but if this ever occurs it must at least be very rare. Baldy reports a case of an ovarian cyst protruding through the inguinal canal. A number of cases of intestinal obstruction, the result of an adherent gut, combined with torsion of the cyst, or the result of a loop of intestine being caught in a long pedicle and becoming strangulated in this way, have been reported. Among the first to report such cases were Rokitansky, Hardy, and Ribbertrapp. Infection of an ovarian cyst by the micro-organisms of an intercurrent disease, such as typhoid fever or pneumonia, have been reported.

It has been the author's intention in this paper to urge the necessity of early operation in all cases of ovarian tumors unless there is some strong counterindication for the same. It has been shown that in these 63 consecutive cases of ovarian tumors that there were 10 cases (15.8 per cent.) of malignancy, 10 cases of torsion, 1 case of rupture, and 1 case of suppuration. In other words, there were 21 cases (1 case of malignancy being combined with torsion) which would surely have died in a short time without operation; how many of the remaining 42 cases would have developed

some fatal complication if operative means had not been adopted it is impossible to say.

In these 63 cases operated upon there were two deaths, one occurring in a case of suppuration of a benign ovarian cyst, and the other in a case of malignant disease. Both were in bad condition before operation and extremely septic. The operative mortality for the 53 benign ovarian cysts is therefore a little less than 2 per cent., the operative mortality for the entire series being about 3.17 per cent.

Conclusions. As regards malignancy.

1. That one in every four to six cases of tumor of the ovaries is malignant, and that this proportion is sufficient to warrant the treatment of all cases of ovarian tumors as malignant until proved otherwise.

2. That the operative mortality in cases of malignant disease of the ovaries should not be above 10 or 12 per cent. That the number of cures at the end of five years will be relatively small. That carcinoma is by far the most frequent and most dangerous of the malignant diseases of the ovaries, and that the recurrences will be largely due to this condition, with the exception of the epithelioma chorioectodermale of Piek, which is probably one of the most malignant of the ovarian tumors, but which occurs much more infrequently than carcinoma.

3. That every case of ovarian tumor should be operated upon at once, unless there is some strong counterindication for the same.

4. That the so-called "border-line cases" should be operated on because the case may present all the clinical evidences of malignancy, and on operation may prove benign, or the gross specimen may even, together with the clinical symptoms, appear malignant, and on histological examination prove benign; this is especially true of adenopapillomata, which frequently grossly and clinically so closely resemble adenocarcinomatous papilloma.

5. That an exploratory laparotomy and the removal of ascites will make many cases more comfortable, and should certainly be performed when there is any doubt whatever as to the absolute diagnosis of malignancy.

6. That all ovarian tumors should be subjected to a rigid microscopic examination, and in cases in which there is any doubt as to the character of the tumor a large number of sections should be taken, and that this routine probably in part accounts for the high percentage of malignancy occurring in the series of ovarian tumors reported in this paper.

Further conclusions.

7. That parovarian cysts are far less dangerous than true ovarian cysts. In this series of 19 consecutive cases of parovarian cysts there were no complications and no malignant degeneration.

8. That torsion, next to malignancy, is the most frequent and dangerous complication occurring in ovarian tumors, and that it occurs in a mild form more often than is generally supposed.

9. That in the 63 cases which have been reported, 33.33 per cent. would surely have died within a short time without operation.

10. That the operative mortality for all ovarian cysts should be under 8 or 10 per cent. In the above series it was 3.17 per cent. That the operative mortality for benign cysts will be much less—in this series it was less than 2 per cent. That the operative mortality for malignant tumors of the ovary should certainly be under 10 or 15 per cent., and that early diagnosis and immediate operation on all new growths of the ovary will greatly reduce this proportion.

Bibliography.

Alberti. Hager's Beitrage, Bd. ix., Heft 3.

Ahrens. Cent. f. Gyn., Bd. xxvii. 1903,

Backhaus, C. Arch. f. Gyn., 1903, Bd. lxiii.

Baer, B. F. At the hospital of the Philadelphia Polyclinic.

Baldy, J. M. American Journal of Obstetrics, New York, 1898, vol. xxxviii.

Ballard, H. G. Journal of the Gynecological Society, Boston, 1870, vol. iii.

Bender. Review de gyn., Paris, 1903, T. vii., No. 4.

Bennett, J. H. Monthly Journal of the Medical Society, London and Edinburgh, 1848, vol. xlix.

Bernays. St. Louis Medical and Surgical Journal, 1880, vol. xxxix.

Beyea, H. G. American Journal of Obstetrics, 1898, p. 872.

Bolt, H. J. American Journal of Obstetrics, 1886, vol. xix.

Breisky. Quoted by Murphy, American Journal of Obstetrics, 1903, p. 753.

Bristowe, J. S. Transactions of the Pathological Society, London, 1860–61, vol. xii.

Charannaz. La gynécologie, June, 1905.

Clark, J. G. American Journal of Obstetrics, 1898, vol. xxxviii.

Cohn, C. Zeit. f. Geb. u. Gyn., 1886, Bd. xii.

Deaver, J. B. American Journal of Obstetrics, New York, 1898, vol. xxxviii.

Demons, G. Bull. et mém Soc. de chir. de Paris, 1887, T. xiii.

Doran, G. Transactions of the Pathological Society, 1884–85, vol. xxxvi.

Emmet, T. G. American Journal of Obstetrics, 1884, vol. xvii.

Fisher, H. M. Boston Medical and Surgical Journal, 1885, vol. cxii.

Flaischlen. Zeit. f. Geb. u. Gyn., Bd. vii.

Fox, Wilson. Medico-Chirurgical Transactions, vol. xlvii. p. 227.

Freund, H. W. Deutsche med. Woch., 1898, Bd. xxiv.

Freund, H. W. Zeit. f. Geb. u. Gyn., 1889, Bd. xvii.

Fritsch. Bericht u. die Gyn. Operationen des Jahrganges, 1891–92.

Fritsch. Bericht aus der Breslaun Frauenklinik., 1891, Bd. lxiv.

Garrigues. Medical Record, 1881, vol. xix.

Garrigues. Diagnosis.

Garrigues. Diseases of Women.

Gelpke, S. Geburt. u. Gyn., Bd. xvii.

Geyl. Arch. f. Gyn., 1887, Bd. xxxi.

Gottschalk, G. Arch. f. Gyn., 1902, Bd. lxv.

Grosse. Verhandl. der Deutsche Gesellsch. f. Chir., Berlin, 1898, Bd. xxvii.

Hall. Canada Lancet, June, 1905.

Hessel. Central. f. Gyn., 1905, No. 20.

Hoerman. Munchener med. Woch., March 21, 1905.

Kelly, H. A. Operative Gynecology.

Kolisko. Med. Jahrbuch, Wien, 1884.

Kratzenstein, G. Zeit. f. Geburt. u. Gyn., Bd. xxxii.

Kratzenstein. G. Zeit. f. Geb. u. Gyn., 1897, Bd. xxxvi.
Kustner, O. Central. f. Gyn., Leipzig, 1884, Bd. viii.
Lenarmant. Ann. gyn. obst., January, 1905.
Leopold. Arbeit aus der Königl. Frauenklinik in Dresden, Bd. ii.
Le Page. Central. f. Gyn., 1905, No. 16.
Lewis, M. J., and Le Conte, R. G. American Journal of the Medical Sciences, October, 1902.
Mathes, G. L. Cincinnati Lancet and Clinic, 1881, vol. vii.
Mayer. Charité annalen, 1882, T. vii.
Mitjukoff. Arch. f. Gyn., 1895, Bd. xlix.
Olshausen, R. Zeit. f. Geburt. u. Gyn., 1885, Bd. xi.
Orthmann. Zeit. f. Geburt. u. Gyn., 1898, Bd. xxxix.
Netrel, W. Nord. Med. Ark., 1885, Bd. xvii.
Peaslee. American Journal of Obstetrics, New York, 1878, vol. xi.
Pick, L. Berliner klin. Wochenschrift, 1904, Nos. 7 and 8.
Pick, L. Central. f. Gyn., 1894, Bd. xxxix.
Pfannenstiel. Münchener med. Wochenschrift, 1905, No. 27.
Pfannenstiel. Arch. f. Gyn., 1895, Bd. xlviii.
Price, M. Proceedings of the Philadelphia Medical Society, Philadelphia, June 30, 1903.
Ratschinsky. Monatschrift f. Geburt. u. Gyn., 1895, Bd. i.
Rissmann. Deutsche med. Wochenschrift, 1905, No. 13.
Royster, H. G. Charlotte Medical Journal, July, 1902.
Rueder. Central. f. Gyn., 1896, Bd. xx.
Runge, M. Central. f. Gyn., 1887, Bd. xi.
Schligtendal. Berliner klin. Wochenschrift, 1886, Bd. xxiii.
Schmaus. Munchener med. Wochenschrift, 1905, S. 1074.
Schult, Th. Arch. f. Gyn., 1901, Bd. lxiv.
Schwartz, G. Arch. f. Kinderkrankheiten, 1901.
Shoemaker. Medical News, March, 1905.
Simpson, J. G. Contribution to Obstetrical and Pathological Society, Edinburgh, 1853.
Skutsch, F. Zeit. f. Geburt. u. Gyn., 1899, Bd. xl.
Smith, A. H. Proceedings of the Pathological Society, Philadelphia, 1867, vol. ii.
Steven, J. L. Glasgow Medical Journal, 1898, vol. i.
Stone, I. L. Washington, D. C., Malignant Tumors, pp. 8–10.
Strassman, P. Zeit. f. Geburt. u. Gyn., 1891, Bd. xxii.
Thomas, T. G. American Journal of Obstetrics, 1871–72.
Tillman, G. Hygiea, 1889, T. li.
Toth. Central. f. Gyn., 1896, Bd. xx.
Uspensky. Zeit. f. Geburt. u. Frauklinik., Bd. lxxxvii.
Vassmer, W. Arch. f. Gyn., 1902, Bd. lxiv.
Von Khantz, Jr., A. Monat. f. Geburt. u. Gyn., 1902, Bd. xvi.
Waitz. Deutsche med. Wochenschrift, 1891, Bd. xvii.
Werder, X. O. American Gynecological and Obstetrical Journal, 1899, p. 397.
Werth. Arch. f. Gyn., Bd. xxiv.
Westemark. Ann. Hygiea, 1889, T. xvi.
Wiel. American Medicine, June 10, 1905.
Williams, J. W. Johns Hopkins Hospital Bulletin, December, 1891.
Williams, J. W. Johns Hopkins Hospital Bulletin, 1893, p. 1.

A SKETCH OF THE LIFE OF THOMAS BOND, CLINICIAN AND SURGEON.[1]

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FOREWORD.

About a year ago I became interested in investigating the career of Dr. Thomas Bond. Because of his active interest in the founding of the Pennsylvania Hospital and in clinical teaching in that same institution I felt I should like to know something about the antecedents, the character, and the general surroundings of a man who did so much to mould the medical thought in the middle of the seventeenth century. I consulted various books that we possess in the College of Physicians, all the biographies available in our public and private libraries, and the various medical histories with which you are doubtless familiar. Few of them contain more than a brief sketch of Thomas Bond. I discovered more information concerning him in Morton's *History of the Pennsylvania Hospital* than from any other one book; this perhaps was but natural, as Bond and his associate physicians, aided and abetted by the shrewd advice of Benjamin Franklin, should certainly receive the credit for founding the Pennsylvania Hospital. I discovered, however, in the College of Physicians six volumes of a co-partnership ledger which gave me the opportunity of studying the character of Bond's daily work and his patients, and these facts further stimulated me to attempt to collect, as far as I could, enough material to round out the following sketch of his life, which, though it is incomplete, may contain some few facts regarding him unknown to some of you.[1]

GENEALOGY.

Thomas Bond, the son of Richard and Elizabeth (Chew) Bond, was born in Calvert County, Maryland, in 1712. His mother, whose maiden name was Elizabeth Benson, was a widow, having primarily married Benjamin Chew, who died about 1700. She married Richard Bond September 24, 1702. This much is known, that Thomas was born in 1712 and Phineas, his younger brother, in 1717. I am unable to discover if there were other children. Although little is known of their early education, it is probable that the brothers received the same advantages in early life. It is known that Thomas studied medicine under the preceptorship of Dr.

[1] Paper read before Historical Section, College of Physicians, Phila. Published by arrangement, simultaneously, in the "Medical Library and Historical Journal."

[1] For many valuable suggestions in securing some of the following information I am much indebted to Miss May Atherton Leach, of the Historical Society of Philadelphia.

Hamilton, a well-known Scotch physician of Calvert County. He subsequently travelled in Europe and spent considerable time in study at the Hotel Dieu at Paris.

It is likely that Thomas Bond came to Philadelphia before 1730 and began the practice of medicine either in 1732 or 1734. He married Sarah Roberts when he was very young, perhaps only eighteen. They certainly had six children, and perhaps more. At this time it is difficult to reconcile all the dates I find in the records of Christ Church, Philadelphia, concerning the baptism of the children born to Dr. Thomas and Sarah Bond. Elizabeth, born July 26, 1730, and baptized September 18, 1745, was the eldest child. Thomas, Jr., born in January, 1737; Thomas, Jr., born in 1743 (this is probably a second son named Thomas); Sarah Rebecca, born January 14, 1744; Phoebe, born November 9, 1748; Robert (Richard ?), born November 18, 1750; Venables, born February 4, 1754, and a second Venables, born January 25, 1765.

Elizabeth married Dr. John Martin on May 9, 1765. Neither he nor his wife lived many years, for I find that Elizabeth died on March 26, 1787, in the Pennsylvania Hospital; there is a note in the hospital minutes: "That in consideration of the eminent services rendered to the Institution by the late Doctor Bond, it is unanimously agreed that no charge should be made for the board of his daughter, Elizabeth Martin, deceased, or for the servant who attended her."

Fig. 1.—Thomas Bond, from an engraving in the College of Physicians, Philadelphia.

Thomas, Jr., the oldest son, married Anne, daughter of Evan Morgan, on May 10, 1764. She died April 6, 1774, a few years after losing her only son, Thomas, whose body is deposited with her in Christ Church graveyard.

Thomas Bond, Jr., took his degree of medicine and entered into practice; in the latter part of 1776 he was appointed a surgeon's mate in the medical department of the army. He seems to have conducted his affairs with ability, for he was promoted, and in 1784 was still commissioned as a purveyor or commissary; he had the rank of Acting General-

Director of Hospitals. His wife had died before the Revolution (1774), and after he finished his military duties he removed from Philadelphia to Morgantown, W. Va. He died at that place December 17, 1793, was there buried, and only some few years ago were his bones disinterred and brought to this city and placed in Christ Church burial-ground.

Sarah (Rebecca) married Thomas Lawrence in 1768.

Phoebe probably died in infancy.

Robert may have also been named Richard, for in Graydon's *Memoirs* (p. 81) I have discovered the following reference: Graydon says he had become intimate with the second son of Dr. Thomas Bond, who lived next door to him. Young Richard had prematurely given up his studies at Princeton College and was giving himself up to the pleasures of the fashionable world. He notes, "He had the most lordly contempt for the opinion of the world, that is, the sober world, of any young man I have known, as well as a precocity in fashionable vices equalled by few and certainly excelled by none." He was handsome in person, being of full chest and highly colored complexion. He is stated to have been a favorite with his father, and studied medicine under his guidance. He died on December 23, 1772, of pulmonary consumption.

The first Venables probably died in infancy. The second was living at the death of his father.

Phineas Bond, Thomas' younger brother, married, in 1748, Williamena, daughter of Colonel the Honorable William Moore, of Moore's Hall, Pennsylvania. (Moore's Hall is still standing and the mansion is at present the residence of Governor S. W. Pennypacker.) Six children were born to them—five girls and one boy. The eldest was Phineas, Jr. Of the five girls two of them only interest us—Williamena and Elizabeth. The former became, in 1779, the second wife of Brigadier-General John Cadwalader, the son of Dr. Thomas C. Cadwalader. Elizabeth, in 1792, married John Travis, Esq., of Philadelphia. One of her daughters subsequently married a Cochrane. Through these two branches of the Bonds the present descendants of the family in Philadelphia came.

HIS EARLY PRACTICE, OFFICE, ETC.

Dr. Bond began the practice of medicine in Philadelphia in 1732,[1] at the age of twenty, and soon associated with him in his work his younger brother Phineas. They soon became active in practice, and we find either one or both of the brothers usually foremost in all enterprises, either municipal or medical. In the event of epidemics of typhus, yellow fever, or ague it was usually Dr. Thomas Bond who was foremost in suggesting methods of attack and relief.

Thomas Bond, according to a *Directory* compiled from the Philadelphia newspapers of 1764-68, lived on Second street near Norris' alley. Norris' alley ran east and west one square from Front to Second street between Chestnut and Walnut streets. There is a continuation of the alley from Second street toward Third street, called Lodge's alley, and the first street north was called Gray's alley. Norris' alley is therefore the first street north of Walnut street and is now known as Sansom street.

On the southeast corner of Second and Norris' alley stood, until a quarter of a century ago, an historical house known as "The Slate-roof House." This house was built prior to 1700 by a prominent citizen named Samuel Carpenter and was the residence of William Penn during his second visit to this country. The house was the first and only one in the city in that time which was roofed with slate. Penn's son John, called "the American," was born in this house, the only one of his family born in this country. Subsequently James Logan lived there, later on William Trent (founder of Trenton) purchased it, and finally it passed into the hands of Isaac Norris in 1717. From 1764 on Mrs. Graydon kept a fashionable boarding house here and entertained many celebrities. It remained a portion of the Norris estate until recent years. It was demolished in 1870. It is probable that Thomas Bond lived just south of this house or in the house on the opposite corner.

Second street at that time was well populated with doctors. John Morgan lived on Second street, as did also John Redman, the first President of this College, and William and James Logan, the well-known lawyers. William Shippen lived at the corner of Fourth and Prune streets.

It must be remembered that at this time Philadelphia was but a village and the streets in many places not paved until 1800. As early as 1750 Franklin was interested in schemes to pave the streets and to light them at night. When Dr. Bond was probably at the height of his reputation the population of Philadelphia was but 28,042 (1769). Ten years before this time there were but thirty-seven four-wheeled vehicles in the city, though single-horse chairs were said to be numerous. There was not at this time any daily paper published, though shortly afterward, in the 70's, a daily paper began to appear. There were several papers published twice or three times a week. The annual death rate a few years after Dr. Bond's death, for instance from September, 1787 to 1788, was but 998; this is perhaps 25 per cent. more than our weekly death rate at present.

During many years of his practice Dr. Bond went about seeing his patients in a two-wheeled sulky drawn by a black horse (Watson's *Annals*). This mode of conveyance was then permitted only to the aged and infirm doctors. Watson stated that the young physician of those days who would have been rash enough to use any mode of conveyance other than his legs would have lost both his reputation and prac-

[1] I have chosen this earlier date though Norris gives 1734.

tice in a short time. Some of the older physicians used to go about on horseback. Thus, Dr. William Shippen, Sr., when a hale and hearty youth of ninety, would ride in from Germantown on horseback to see his patients in the city. It is stated that this gentleman was never known to have worn an overcoat at any time. A protection for the body in bad weather was not over-sufficient in those days. Those who had to work in the open in bad weather wore a long cape, which was lined with a sort of rubber cloth, with a hood having a projecting rim of the same material. It will be remembered that umbrellas were unknown at this time, and that Dr. John Morgan was the man who insisted upon their introduction as a matter of common sense, and he was the first to carry an umbrella in Philadelphia.

In the earlier years of his practice Bond probably did a good deal of work among the poor. The population of Philadelphia was rapidly increasing by immigration, and the authorities found it necessary to establish a form of detention house or lazaretto, on Province Island, below the city, down the Schuylkill River. Men who were his intimate friends were appointed physicians of the port: Dr. Patrick Baird, in the early portion of the century, followed by Dr. Thomas Graeme, and subsequently Dr. Lloyd Zachary. The brothers Bond doubtless had considerable experience, therefore, with the epidemics of yellow and typhus fever, which were introduced into Philadelphia through the medium of the immigrants. Bond refers to five epidemics in his introduction to his clinical lectures.

It has already been stated that Thomas Graeme and Lloyd Zachary were physicians of the port in Philadelphia. There is ample evidence to show that the Governor constantly requested Dr. Thomas Bond to accompany either one or the other of these physicians on board of suspected vessels. Thus, September, 1741, "Doctors Lloyd Zachary and Thomas Bond, having by order of the two members of the Board, visited the ship St. Mark with Palantines from Rotterdam, and reported the same to be sickly and to have infectious disease on board, it is ordered that the said ship remain at least one mile's distance from Philadelphia without landing any passengers or baggage till further orders." (*Colonial Archives*, vol. iv. p. 496.) In the following year Bond certifies to the state of health on board the *Constantine* "and that the vessel has been cleansed and aired in the likeliest manner." It is more than probable that Bond held this position of Inspector or Assistant Inspector for quite a number of years, and in 1747 he, in conjunction with Dr. Graeme, made a full report to the Council of Safety concerning the condition of contagious disease on board the ship *Vernon;* in this report they make numerous recommendations as to the isolation of sick patients and the fumigation and cleansing of houses in which illness has occurred.

If there was illness of a contagious nature on board vessels at that time it was customary to detain the vessels at Province Island and subsequently transfer the passengers to the pest house or lazaretto. In 1749, when Bond after having visited a vessel discovered contagious disease, the pest house was found to be in such miserable order that Councils recommended refurnishing and the building of outhouses for the accommodation of patients. In 1756 Bond acted as Coroner to Philadelphia city and county, being elected by the returns of October 4, 1756. I cannot ascertain how long he held this office.

The following are letters between Bond and the Council, written in November, 1754, relating to business in the port:

"Doctor Graeme and I have spent this Day in examining the Palatines that have been Landed in and near the City, and shall as soon as possible give his Honour the Governor a particular Account of the Condition in which we found them, the Persons that nursed them, and the People living in the Neighbourhood of their Habitations; but the Security of the Citizens requiring the immediate removal of two Companies of them, I think it my Duty to give you this early Notice, that in the House of Philip Burcort, near the reformed Church, a considerable number of them, belonging to Daniel Benezett, are in a weak and diseased State, and are confined in so small a Room that the Air, etc. about them is in a high Degree of Putrefaction, and two of the Family are now ill of putrid Fevers. The People in the House of Frederiek Burk, at Spring Garden, are circumstanced in the same manner; they belong to Henry Kepler. 'Tis my opinion that both the diseased and healthy Persons in both these Houses shou'd be removed to a considerable distance from the City, and care taken to purify the Houses well before other Tenants are permitted to go into them.

"Tho. Bond."

Then follows a detailed report of the examination of the above houses and a discussion as to the character of the disease they were studying (probably a typhoid fever), and the conclusion that it was of a non-contagious type, and they end with this plea:

"We cannot conclude this Resolution without saying our case is really a bad one, since a Security from Contagious Diseases is expected of Us, and the Legislature has not made the necessary regulations to prevent malignant Disease being generated by these people after they come into Port, where there is much more danger of it than at Sea.

"Thos. Graeme.
"Thos. Bond."

During the early part of Dr. Bond's practice there was erected between Third and Fourth and Spruce and Pine streets the Almshouse, or what was properly known as "The Bettering House." About the middle of the century a much larger building was erected west of the Pennsylvania Hospital between Ninth and Tenth streets. There is no question about it that this institution had a hospital ward and that physicians were probably in attendance, but there is no record whatever that distinctive appointments of doctors were made until May 18, 1769, "when Dr. Cadwalader Evans and Dr. Thomas Bond were re-elected at a salary of Fifty Pounds a year, out of which they were required to furnish such medicines to the inmates as might be needed."

(Packard's *History of Medicine in the United States*, p. 324.) It is altogether probable, however, that the Almshouse had a sick ward when it occupied its first site in the "Green Meadows." In 1770 the Managers of the Almshouse permitted Dr. Bond and Dr. Evans to instruct students in an obstetrical clinic, and this has been called the "first obstetrical clinic." In 1774 additional eminent physicians, such as Kuhn, Rush, Dutfield, Clarkson and Parke, were appointed to the staff, and so the hospital department became of first importance, both to the sick poor and as an adjunct to the new medical school. As late, however, as 1802 negotiations occurred between the Poor Directors and Hospital Managers about admission of patients from the Almshouse to the hospital. Morton considers it unlikely that they had medical wards till 1815.

He was justly celebrated as a lithotomist. He probably performed the first operation of this kind in America, although the credit has been given to Dr. Jones, of New York. There is no question, however, that Dr. Bond performed this operation successfully as early as October 29, 1756, in the Pennsylvania Hospital, and many times subsequently. An interesting light is thrown upon his skill as an operator by a contemporary writer in 1772, not a physician, and whose identity is unknown:[1] "I had the curiosity last week to be present at the hospital, at Dr. Bond's cutting for stone, and was agreeably disappointed, for instead of seeing an operation said to be perplexed with difficulty and uncertainty, and attended with violence and cruelty, it was performed with such ease, regularity, and success that it scarcely gave a shock to the most sympathizing bystander, the whole being completed, and a stone of two inches in length and one in diameter extracted in less than two minutes." "If," adds the writer, "surgery is productive of such blessed effects, may we not with Cicero justly rank it among the first of arts and esteem it worthy of the highest culture and encouragement?"

The following reference to the personality of Thomas Bond is found in a letter written by Charles F. Weisenthal, M.D., of Baltimore, to his son Andrew, who was studying medicine in Philadelphia during the year 1781-82, two years before the death of Bond. He says:

"I am glad you have introduced yourself to Doctor Bond though he may have some Oddities, you may nevertheless rely on this that his Acquaintance will be valuable to you, both his Learning and Experience are unquestionable, and he moreover is very communicative and takes a Delight in instructing young Persons, and that in proportion to their Diligence and Application, you will therefore visit his Lectures frequently and freely apply to him to resolve such things as may be obscure to you, he is a good Surgeon besides and may give you some good hints in the hospital."

[1] Norris' History of Medicine in Philadelphia, p. 26.

About a good thing, however, there may be a difference of opinion; in a letter from Dr. Barnabas Binney (the father of Horace Binney) to a friend, written in 1778, from a general hospital near Philadelphia, and filled with more or less gossip about his medical confreres, he says: "Kuhn, Rush, and old Bond I hear intend to Lecture in ye Winter. Thank God I am done with them." (*Penna. Mag.*, vol. ii. p. 467.)

I have discovered that Thomas Bond in 1769 owned one hundred and twenty-four acres, four horses, four cattle, had three servants, and was taxed annually one hundred and sixty-nine pounds, ten shillings. Several years later he had increased his horses to six and cattle to ten. In the year 1780 the valuation of Dr. Thomas Bond's various properties in the Middle and Walnut Wards and the eastern and western parts of the Northern Liberties reached $208,000. He seemed to own about 400 acres of real estate at that time.

Phineas Bond, who was five years younger than Thomas, enjoyed the same preliminary education, but secured a more extensive European advantage than did his brother, for he studied for a considerable length of time at Leyden, Paris, Edinburgh, and London. According to Thacher, "He was not less disposed to form than well qualified to judge of every understanding for the improvement of the medical character of his country." He did not attempt to do any surgery and should be called a practitioner of internal medicine. He seems to have been a man of great personal charm, and according to Wistar's estimate no medical man in Pennsylvania "ever left behind him a higher character for professional sagacity or for the amiable qualities of the heart." He was one of the founders, together with Thomas Hopkinson, of the College of Philadelphia, now the University of Pennsylvania. He was also an original member of the Philosophical Society. Thacher quaintly says, "He was remarkable for conviviality but never habituated to intemperance."

PATIENTS AND PRACTICE.

The character of Dr. Bond's patients can be surmised from a study of his ledger, six volumes of which are to be found in the library of the College. These books are the daily records of the mutual practice of Drs. Thomas and Phineas Bond, and are labelled in ink on the outside "Co-Partnership Ledger of Drs. Thomas and Phineas Bond." They are long, narrow, leather-bound books, resembling the present-day cash books, and containing the accounts of the brothers from 1756 to 1770. In the first four volumes there is no daily visiting list, but in the last two volumes there is a daily list of visits and subsequent compilation of the individual accounts. Among his patients are to be found families whose names are still familiar in Philadelphia. I will mention some few of them:

B.I.G.D.

Stephen Anthony, Thomas Austin, James Bard, John Bayly, James Biddle, John Burr, Nathaniel Chapman, James Claypole, Nathan Cleves, Henry Clifton, Jacob Cox, Benjamin Chew (Recorder), Joseph Davenport, William Duffield, Nathan Edwards, Jonathan Evans, Tench Francis (Recorder), Benjamin Franklin, William Franklin, George Gray, Alexander Graydon, John Guest, Alexander Hamilton, David Hamilton, Capt. John Hamilton, John Humphreys, John Inglis, Benjamin Kendall, Lynford Lardner, John Lober, James Logan, Thomas London, Jonathan Mifflin, Capt. Samuel Mifflin, Robert Morris (Financier), Samuel Morris, John Ord, John Palmer, James Payne, Israel Pemberton, Barthol. Penrose, Edmund Physic, Samuel Purveyance, Thomas Redman, Thomas Ritchie, Hugh Roberts, William Rush, Edward Shippen, Jr., Atwood Shute (Mayor), Enoch Stone, John Swift, Spencer Trotter, Richard Tyson, Col. Washington (George?) Joseph Wharton, Jr. (Recorder-Mayor), Daniel Wister, Richard Wister, Mordecai Yarnall, John Yeates, and Thomas York.

He seems to have done all varieties of surgery. I find records as follows:

"Opening breast and sundry dressings."

"Reducing and setting his son's fractured arm."

"Operation for fistula lacrymalis."

"Sundry dressings to his Dutch boy's fractured skull."

"Laying open and sundry dressings to his imposthumated liver."

"To scarifying his negro's mortifying feet, dressings, etc."

"To a visit to his place in ye night and delivering his negro woman of a difficult birth."

There are also records of several castrations. He operated on May 27, 1765, on James Child, Jr., for stone, which was as large as a hen's egg and weighed 2 ounces, $2\frac{1}{2}$ drachms. On December 10, 1765, he operated on a child of seven, Jeremiah Tracy, and removed a stone 1 ounce and 5 drachms in weight, which measured $1\frac{1}{2}$ inches in diameter and $1\frac{7}{8}$ inches in length.

He also did amputations, for in July, 1765, he amputated the leg of a negro named "Cuff," who was discharged later in the month cured. The negro's master paid the steward 60 pounds for board.

Some of the charges in his ledger are interesting. As is well known to you the attending physicians usually furnished the drugs, for which charges were made, and Dr. Bond was no exception to this rule. Dr. John Morgan was probably the American Lydgate to request his patients to secure his prescriptions at the drug store. I find charges for "Hausta anodyne," "gutta stomachicie," "antispasmodic julep," 3/ 6*d;* "digestive ointments," "phlebotomies," and "epispastica," etc.

I can find no record of any abdominal operations. He, however, did perform paracentesis probably both on the chest and abdomen. It is apparent from a study of his work that he was a practitioner who believed in freely laying open abscesses or superficial growths. The prevalence of smallpox, especially among children, is also noted. He was up to date enough to practice inoculation, even though this operation was not yet fully regarded with confidence. He seems also to have been competent to diagnose measles.

I have found in Volume IV. of the accounts in the year 1765 one or two quaint charges. "To my advice, attendance, and to hemorrhage spitting, 1 pound, 7 shillings;" "To opening her thigh, my advice, long and diligent attendance to her under several severe fits of illness, 2 pounds, 14 shillings." It is also evident that he either scarified or used incisions for the removal of dropsical effusions in the legs, as I find an item, "To tapping his legs, 10 shillings."

He was charitable. I find an account against a woman for 3 pounds 6 shillings and 8 pence, upon which was paid 1 pound and 18 shillings, with the following remarks: "The rest remitted—a poor widow."

In Dr. George W. Norris' account of *The Early History of Medicine in Philadelphia,* p. 27, he states that Dr. Rush attributed to Dr. Bond the introduction and general use of mercury in practice in Philadelphia. He prescribed it in all diseases which resisted the common modes of practice. At this period bathing with either hot or cold water was but little employed in the treatment of acute diseases, and Dr. Bond is said to have been a liberal user of not only hot and cold baths, but vapor and warm-air baths, both of which he introduced into the practice of the Pennsylvania Hospital. This use of water was much more extensively employed later by Dr. Benjamin Rush.

Dr. Bond devised several surgical appliances; the one best known to us at the present time is the so-called Bond splint, which has been used many years, and in some hospitals still, for the treatment of fractures at the lower end of the radius. He also devised an instrument for the removal of foreign bodies from the œsophagus.

At a time when moving from house to house could not have been accomplished with any great ease, Dr. Bond seems to have been capable between the 60's and 70's of making at any rate from twelve to sixteen visits a day.

I find records in Dr. Bond's book of consultations with almost all of the prominent practising physicians, Thomas Graeme, William Shippen, Sr., Dr. Kearsley, Cadwalader Evans, etc. There is reason to think that Bond not only attended but charged physicians and clergymen, as he has accounts against them which seem to have been settled. His ordinary charge for a phlebotomy was 2/ 6*d.* He did a great deal of inoculating, and, as has been before stated, his charges for this service were high (To Mr. ——, inoculating his child, medicines, and attendance, £4 1*s*). He had great numbers of military men on his book, captains and colonels.

He visited many of the suburbs, going as far as Haddonfield, Mt. Holly, Gloucester, Chester, Darby, Mareus Hook, and John's Woods. It can therefore be seen that his practice included many of the more prominent people of Philadelphia, for many of the names given above are of men prominent in government, banking, business, and social life.

It is probable that during the troublous times before the Revolution both Thomas and Phineas Bond were Loyalists. Phineas, you may recall, died in 1773. In Sabine's *Biographical Sketch of Loyalists*, p. 236, I find sketches of both Thomas and Phineas Bond; he quotes a letter from Chief Justice Shippen to his father at Lancaster, written January 8, 1758, as follows:

"Our assembly have taken up William Moore and the Provost, and put them into custody for writing a libel against the former assembly. Thomas Bond and Phineas (Bond) were on the point of being committed on the same account. The latter was actually in custody of the Sergeant at-Arms, but afterwards discharged. How the matter will end is yet uncertain."

As the Revolution drew near it is probable that Thomas became more weak-kneed in his opinions and finally became a Whig. It remained for Phineas Bond, Jr., however, to become an active Loyalist or Tory and I find in the *Pennsylvania Colonial Records*, vol. xi. p. 284, evidences that Phineas, Jr., was included among those "who have in their general conduct and conversation evinced a disposition inimical to the cause of America." In the following month Dr. Thomas Bond requested that Phineas Bond, Jr., be permitted to go to Virginia under parole and from thence to the West Indies; this was granted. The following year Phineas, Jr., was held on his parole. He was considered guilty of high treason and his property confiscated, for I find records of debts against the estate of Phineas Bond, forfeited to the Commonwealth by his attainder of high treason in 1787. In May, 1787, there is an acknowledgment by Congress of the appointment of Phineas Bond as Consul for His Britanic Majesty from the Middle States. The following year he returned to America, continued in office for a considerable number of years, and subsequently died in 1812 in England.

LITERARY WORK.

There is but little of his literary work to be discovered. I have found one article of his, published in 1754 in *The Medical Observations and Inquiries*, vol. i. p. 68, with a most unusual title, as follows: "A Worm, and a Horrid One, Found in the Liver." This article is a letter written to Dr. Clephane, of London, describing a case occurring in a Mrs. Holt, of Philadelphia, detailing her symptoms, which extended over about eighteen months, the passage of a supposed intestinal parasite, description of the autopsy accompanied by an engraving of the postmortem appearance of the abdomen and the supposed worm. The case impresses me as probably one of subphrenic abscess or abscess of the liver. I have no knowledge of such a parasite existing as is depicted in the illustration. That he wrote other articles is certain, yet it remained for the Managers of the Pennsylvania[1] Hospital to preserve in full his introductory lecture to a course of clinical lectures delivered at that hospital. This lecture was primarily read at his own house November 26, 1766, to the Managers and some of the physicians of the hospital and thirty students, and was probably re-read at the hospital on December 3, 1766, at the inauguration of the clinics. The Managers thought so highly of it that it was spread in full upon the minutes and only in that way preserved. It is to be found in full in the *History of the Pennsylvania Hospital*, by Thomas G. Morton, and was also republished in 1827 by Paul Eve, a then student of the Pennsylvania Hospital, in the *North American Medical and Surgical Journal*, vol. iv., and is copied in full in Norris' *History* and also in F. R. Packard's work.

A second paper in the *Medical Observations and Inquiries*, vol. ii. p. 265, by Thomas Bond was "On the Use of Peruvian Bark in Scrofulous Cases." In Atkinson's *Medical Biography*, p. 312, under the head of "Bond" (without first name) "An 8vo: Essay on the Incubus or Night Mare, published in 1753." His comments on this article are remarkable: "A bond in judgment against sleep, and a very awkward mare to ride. She generally has the upper hand of the jockey, turning the gray mare into the better horse. But the great misery is, that this happens in the dark, and there is nobody to help him—do not buy such a mare—*caveat emptor*."

In addition to the previous papers Bond made quite a number of communications, usually of a medical nature, before the Philosophical Society; thus, on August 16, 1771, he read a letter from Dr. Normandie regarding "A Case of Abscess of the Lungs of Long Standing, Attended with Very Alarming Symptoms, Remarkably Relieved during This Season by Drinking and Bathing in the Bristol Waters." On June 17th, the following year, he read an essay on (*a*) "Epicacuanhæ;" (*b*) "A Description of Plants at the Cape of Good Hope (Dr. Burgeus);" (*c*) "Dr. Landiford's Account of the Epidemic at Barbadoes." In 1779 he read a paper on "The Means of Pursuing Health and Preventing Disease." Two years before his death (on May 21, 1782) Bond delivered the Annual Oration at the State House before the Philosophical Society; he began as follows: "The principal Settlers of Pennsylvania were Emigrants from Great Britain and Ireland, who quitted their native Countries, Beds of Ease and Fields of Plenty, underwent the Perils of a wide and

[1] See the inscription on his tomb, and letters to the Managers of the Pennsylvania Hospital.

boisterous Sea, risked the Barbarity of Savages, and located themselves in Deserts and Forests, filled with deadly Serpents and Beasts of Prey, solely for the Enjoyment of Religious Liberty.

"And as they brought with them the Principles of Peace and universal Benevolence, an inviolable attachment to Justice, and a striking Purity of Manners, they soon softened the Pagan Hearts of the Natives to such Humanity and Affection, that they gave up to them their Caves for Habitations, supplyed them with food, and even robbed their own children of the Mothers Milk to support and cherish their languishing Infants."

He then gives a hasty sketch of the origin of the Philosophical Society, and passes on to the subject of his Oration: "The Rank and Dignity of Man in the Scale of Being" and the sub-title "The Conveniences and Advantages He derives from the Arts and Sciences, and A Prognostic of the Increasing Grandeur and Glory of America, founded on the Nature of the Climate."

The address concludes as follows: "Military Fame may be won or lost in an hour, but the Fame of Science is a character of Duration. It is the Child of a thousand years, approaching slowly to Maturity, and is long in dying."

"The Fame of America must rest on a broader basis than that of Arms alone. Is the just, mild, generous, grateful and learned, as well as brave, will soon be the Enquiry of the World. Curiosity, which leads Mankind to know every minute Circumstance of a new Character, will naturally excite these Questions, and we cannot too seriously reflect, that our Consequence Abroad, depends on our preserving a noble, generous and *unspotted character* at Home."

This is a small book of 34 pages, and the address is distinctly scholarly; barring a few references to the use of new instruments for the measurement of atmospheric pressure, temperature, etc., which he always considered of great importance, there is little reference to things medical.

HIS INTEREST IN THE PENNSYLVANIA HOSPITAL AND MEDICAL INSTRUCTION IN THE SAME.

It is probable that Dr. Bond, from the nature of his practice, daily realized the help and aid that a hospital with its appliances, dressers, nurses, etc., would be to him in his work. It is an assured fact that he certainly talked to his patients and his friends more or less constantly about his hopes of the foundation of a hospital for the care of the sick and injured, to say nothing of the care of the insane, for really during the first years of the hospital much of its work consisted in the care of the so-called "lunatics." There were, however, other physicians who were equally as interested and anxious to aid in such a worthy project. At this time the prominent practitioners in Philadelphia included Drs. John Jones, Graeme, Cadwalader, Moore, Redman, Chovet, Lloyd Zachary, Witt, Kearsley, Jr., and Colden. It was not, however, until Bond approached Benjamin Franklin and explained to him the value that such an institution would be to the community, that any material progress was made in the scheme of the foundation of a hospital. Franklin in fact has often been credited with the honor of being the founder of the Pennsylvania Hospital, but he settles this question positively in his *Autobiography*, in which he says:

"In 1751, Dr. Thomas Bond, a particular friend of mine, conceived the idea of establishing a hospital in Philadelphia (a very beneficent design, which has been ascribed to me, but was originally and truly his), for the reception and cure of poor sick persons, whether inhabitants of the province or strangers. He was zealous and active in endeavoring to procure subscriptions for it; but the proposal being a novelty in America, and at first not well understood, he met with but little success.

"At length he came to me with the compliment, that he found there was no such thing as carrying a public-spirited project through without my being concerned in it. 'For,' he said, 'I am often asked by those to whom I propose subscribing, "Have you consulted Franklin on this business? And what does he think of it?" And when I tell them I have not (supposing it rather out of your line) they do not subscribe, but say they will consider it.' I inquired into the nature and probable utility of the scheme, and receiving very satisfactory explanation, I not only subscribed to it myself, but engaged heartily in the design of procuring subscriptions from others. Previously, however, to the solicitation, I endeavored to prepare the minds of the people by writing on the subject in the newspapers, which was my usual custom in such cases, but which he had omitted."

Bond's interest in the promotion of the Pennsylvania Hospital in its early days is everywhere evident from the minutes of the Managers; thus, on September 5, 1751, "The President and Thomas Bond are requested to consider some of the methods to begin the hospital in a private house so as to accommodate a few patients in order that at least some good might be doing in the meantime until the hospital is built." (Morton's *History*, p. 27, 28.) The house of Judge John Kinsey, on the south side of Market street below Fifth (in 1811 known as 172 High street), with its gardens, pasture, and stable were leased for a sum of forty pounds per annum and twenty-five pounds were appropriated for repairs upon the same. This sum was subsequently found insufficient and one hundred and fifty pounds had to be borrowed from the one thousand pounds of the Provincial Grant. Then came the question of the selection of physicians, and on October 23, 1751, we find that "Doctor Lloyd Zachary and Doctors Thomas Bond and Phineas Bond signified their willingness to give their attendance gratis in taking care of the sick as physicians and surgeons for the first Three Years."

The temporary hospital received its first patient on February 10, 1752. It was an imposing occasion, for on this day a special meeting was called to consider the application for admission of patients into the wards for treatment. "Doctors Graeme, Cadwalader, Moore, and Redman were invited to meet the attending Managers and attending physicians to assist in the selection of the most deserving cases." Margaret Sherlock's disorder was considered relievable and her case suitable, so this woman was the first admission and she was also the first discharged cured. Alice Courent was engaged as a maid or nurse at ten pounds per annum. Subsequently "Israel Pemberton and Thomas Bond were desired to look out for a suitable matron to take care of the house and the sick that shall be placed there." (Morton's *History*, p. 28.)

The attending physicians were, by the rules, supposed to attend the hospital Mondays and Thursdays every week at ten o'clock in the morning, where they met the visiting Managers, admitted cases, etc. It was a rule of the hospital that prior to admission of patients they must be visited by the attending physicians. This practice seems to have been followed for many years. It must have taken a grievous amount of time, and finally the staff rebelled, for in 1802 a request, seconded by Benjamin Rush, Philip Syng Physic, John Redman Coxe, Benjamin Smith Barton, and Caspar Wistar, Jr., was sent to the Managers, suggesting that this rule be dispensed with "on account of numerous and prior engagements of said physicians," and asking they be permitted to send an assistant for the purpose of visiting and examining the sick applicant. The Managers refused this request. With the birth of the hospital the following curious resolution was passed, showing the characteristic prudence of the Managers; it stated that the attending physicians "shall first give demonstration of their skill and ability in anatomy, operations, dressings, and bandaging before the Managers and such others as the Managers might see fit." It is doubtful if this rule was ever enforced.

It may be opportune to remind you of several of the astute methods practised by Franklin in his attempt to secure the passage of an appropriation for the hospital by the Provincial Assembly. He was desirous to secure an appropriation of about £2000, and he felt positive that such a sum would probably not meet with approval. He therefore adopted the sagacious scheme, now so frequently utilized by Andrew Carnegie, of asking the Assembly to grant the sum if the promoters of the hospital scheme would raise a similar sum among those interested in the project. As a matter of fact Benjamin Franklin and the hospital's friends had already more than that sum pledged, and the Provincial Assembly when such a proposition was made to them eagerly swallowed the bait and passed the bill without any objection, little thinking that the money so awarded to the hospital would be picked up at once and utilized. Another of the objections raised to the hospital was that they could not afford to pay the physicians for their attendance upon the sick. Franklin met this objection by the announcement that the physicians had offered "to attend the patients for nothing and supply all the medicine for three years at their own expense." This generous example, set by the brothers Bond and Lloyd Zachary, has been followed by generations of their successors, and practically by all other hospital physicians and surgeons since that time throughout the entire United States.

So the hospital began its life, and Bond was active in all its departments; he saw the necessity of introducing students into the wards and soon had a class of ward dressers following at his heels. These students were charged a small sum for the privilege and the money secured in this way was turned in to the Managers and placed in the so-called "Medical Fund," which became the nucleus of the purchase of the library. This fund in subsequent years became large and was used not only for the purchase of books but at times for some of the hospital improvements. Bond also drew up the certificates presented to the students as an acknowledgment of the completion of a course of attendance upon the hospital clinics. He was also active in securing drugs and finally importing a druggist and the establishment of the drug store.

He was deeply impressed with the necessity of clinical instruction for medical students and had probably repeatedly urged this matter upon the attention of the Managers of the hospital. It was not, however, until 1766 that his suggestions were acted upon by the Managers, and a regular course of clinical lectures begun. He courteously invited the Managers to his house to hear his "Essay on the Utility of Clinical Lectures." This he read in the presence of the Managers, several physicians, and thirty students on November 26, 1766. His arguments seem to have overcome whatever objection they had to a course of clinical instruction, and the introductory lecture was probably a repetition of the essay. It was read at the hospital on December 3, 1766. This essay embodies so much that is good that I shall here give a short abstract of it:

"When I consider the unskilful hands the Practice of Physic and Surgery has of necessity been Committed to, in many parts of America, it gives me pleasure to behold so many Worthy Young Men, training up in those professions, which, from the nature of their Objects, are the most interesting to the Community, and yet a great pleasure in foreseeing, that the unparallel public Spirit, of the Good People of this Province, will shortly make Philadelphia the Athens of America, and Render the Sons of Pennsylvania, reputable amongst the most celebrated Europeans, in all the liberal Arts and Sciences. . . .

"No country then can be so proper for the instruction of Youth in the Knowledge of Physic, as that in which 'tis to be practised; where the precepts of never failing Experience are handed down from Father to Son, from Tutor to Pupil."

He commends the teaching of anatomy, physiology, and the theory and practice of medicine, but feels they must be supplemented by clinical teaching.

"There, the Clinical professor comes in to the aid of Speculation & demonstrates the Truth of Theory by Facts; he meets his Pupils at stated times in the Hospital, And when a case presents adapted to his purpose, he asks all those Questions which lead to a certain knowledge of the Disease, & parts Affected, this he does in the most exact and particular manner, to convince the Students how many, & what minute Circumstances are often necessary to form a judgment of the Curative indications, on which, the Safety & Life of the Patient depend, from all which Circumstances and the present Symptoms, he pronounces what the Disease is, whether it is Curable or Incurable, in what manner it ought to be treated, and gives his reasons from Authority or Experience for all he says on the Occasion; and if the Disease Baffles the power of Art, and the Patient falls a Sacrifice to it, he then brings his knowledge to the Test, & fixes Honour or discredit on his Reputation by exposing all the Morbid parts to View, and Demonstrates by what means it produced Death; and if perchance he finds something unsuspected, which betrays an Error in Judgment, he like a great and good Man, immediately acknowledges the mistake, and, for the benefit of survivors, points out other methods by which it might have been more happily Treated; The latter part of this Field of Tuition is the surest method of obtaining just Ideas of Diseases."

This is an exceptionally fine argument for the study of clinical medicine; it shows also the type of man that Bond was, perfectly willing to acknowledge his mistakes and to benefit by a study of morbid anatomy at all times. He further comments upon the necessity and usefulness of autopsies; states that the only objection to North America as a place to live is that the climate is sometimes productive of severe epidemic diseases in the summer and in the fall, and he feels an attempt should be made "to wipe this stain out of the American escutcheon." He further discourses on the difference between yellow and typhus fever and the agues, and the necessities for their very careful study, so that isolation, prevention, etc., may be accomplished. He remarks on some of the methods for preventing diseases, such as the wearing of flannel shirts (this, you may recall, was a fad of Benjamin Franklin); the use of sassafras bark, and the use of certain chalybeate springs in the treatment of these diseases. His concluding paragraph is as follows:

"I there purpose to meet you at stated times here, & give you the best information in my Power of the nature & treatment of Chronical Diseases, and of the proper management of Ulcers, Wounds & Fractures, I shall show you all the Operations of Surgery, & endeavour, from the Experience of Thirty Years to introduce you to a Familiar acquaintance with the acute diseases of your own Country, in order to which, I shall put up a compleat Meteriological Apparatus, & endeavour to inform you of all the known Properties of the atmosphere which surrounds us, & the effects its frequent variations produce on Animal Bodies, and confirm the Doctrine, by an Exact register of the Weather, of the prevailing Diseases, both here, & in the Neighbouring Provinces, to which I shall add, all the interesting observations which may occur in private practice, & sincerely wish it may be in my power to do them to your Satisfaction."

These clinical lectures were successful in attracting students and with the exception of the interruptions of the troublous times of the Revolution and the Rebellion, have been continued by Bond's successors down to the present day. The attending students were primarily charged a guinea for the year's attendance (1766). In 1774 this sum was raised to five pounds to all students not apprenticed to physicians. In the first year sixteen students attended the clinics, and thirteen pounds, twelve shillings were turned in to the Managers by Dr. Bond, and thus become the nucleus of the Medical Fund. Again, in the year 1769-70, a list of sixteen students was handed in to the steward by Dr. Bond.

About this time also Dr. Bond requested permission to establish a meteorological apparatus in one of the hospital rooms and in this same letter to the Managers he stated: "A neat copy of which (epidemic diseases) with an account of all the curious cases which presented in the hospital, I will annually deposit in the library for the perusal of Posterity." I have searched the older volumes of the library in the Pennsylvania Hospital but have been unable to find these records. It would indeed be intensely interesting if they could be discovered, as they probably would give us definite ideas as to the methods of physical examination and modes of treatment used at that time in the Pennsylvania Hospital.

This time, that is 1765, marked the beginning of systematic medical instruction in the United States; this year's courses in anatomy and surgery (and midwifery) were given by William Shippen, Jr., and lectures on physics by John Morgan. Dr. Bond taught clinical medicine the following year, and continued to hold clinics at the Pennsylvania Hospital till his death. As will be remembered the appointment of Morgan and Shippen was soon followed by that of Rush and Kuhn to the respective chairs of Chemistry and Materia Medica and Botany. Bond was, however, at this time a man of fifty-four, whereas his associate professors were all men of thirty, or under, years of age.

At the foundation of the medical school "It is pleasant to contemplate the attitude of the older practitioners toward

these younger and more cultivated brethren. The elections were reported to have been unanimous, notwithstanding that among the Board of Trustees were all of the old leading physicians. It looks well that after a course of lectures by these two young men (Shippen and Morgan) the veteran Thomas Bond came in from the Pennsylvania Hospital and began his course of clinical lectures." (Scharf and Westcott, vol. ii. p. 1588).

SERVICES IN THE MEDICAL DEPARTMENT OF THE COLONIAL ARMY.

Bond was appointed, together with Drs. Cadwalader, Richard Rush, and Wm. Shippen, Jr., on January 9, 1776, as one of the examining surgeons of the Colonial Medical Department. The Council ordered that no certificates were to be granted to surgeons coming up for examination unless signed by three of the above men. His son, Thomas Bond, Jr., was a surgical mate in the army and had charge in 1776 of the wounded at Elizabethtown, New Jersey. From thence he wrote to his father, then in Philadelphia, asking him to consult General Mifflin regarding the establishment of hospitals for the sick at Darby, Chester, Marcus Hook, Wilmington, and Newcastle. The senior Bond at once wrote to the Council of Safety, December 4, 1776, suggesting "that the Pennsylvania Bettering House and the Provincial Hospital may accommodate them," coupled with other suggestions regarding means for their medical care, provisions, drugs, etc. (Toner's *Medical Men of the Revolution*, pp. 52, 53.) The following day the Council resolved "That the Pennsylvania Hospital be taken up and employed for the sick troops of the Continental Army in compliance with the request from Congress that the said troops be provided with medicines and every necessary." (*Pa. Colonial Records*, vol. xi. p. 34.)

It is probable that both father and son were active in organizing the hospital system in and about Philadelphia. "The senior and junior Drs. Thomas Bond rendered efficient aid in organizing the hospital system on a proper basis and securing competent surgical and medical aid." (Scharf and Westcott, vol. i. p. 332.)

Dr. Thomas Bond, Jr., A. D. C. of the Continental Hospital, appears in the records of the Pennsylvania Hospital in September, 1778, applying for the admission of a large number of convalescing soldiers to the Pennsylvania Hospital, to remain under the care of their physicians and surgeons, to which proposition the Managers objected. Later on, in April, 1779, Dr. Bond, Jr., again requested the use of the lower ward and corridor for convalescing soldiers for a period of not longer than six weeks, which was granted, and we find on June 16th of the same year Dr. Bond, Jr., returning thanks for the use of the hospital for that purpose. Again, in July, 1781, Dr. Thomas Bond, Jr., proposed that "all the British prisoners now sick in the jail, about ninety of them, be admitted as pay patients, and in future all the sick belonging to the army or any of their sick persons shall at all times be admitted on the same footing; the number would average about 40 or 50." The Managers informed him that no malignant disease could be admitted, and his reply was that "they must take all or none." In November, 1783, he made a personal application to have "all the diseased soldiers, their wives and children now in the Continental Hospital, admitted to the Pennsylvania Hospital upon the usual terms," which the Managers declined to do. As far as the Pennsylvania Hospital records are concerned, the last we hear of Dr. Bond, Jr., are letters from Robert Morris, December, 1783, relating to an application made to the last Board by Dr. Bond, Jr., for admission of a number of diseased Continental soldiers whom they agreed to admit subject to the rules of the hospital.

During the Revolution I find that Bond used ordinary powder for disinfection of the hospitals. In March, 1779, he was granted by Councils two pounds of powder to be burned in disinfecting the Work House.

OFFICIAL RELATIONS TO SOCIETIES, INSTITUTIONS, ETC.

Thomas and Phineas Bond were both original members of the Society for the Promoting of Useful Knowledge among the British Plantations (1744). You may recall that the other founders of this Society were John Bartram, the botanist; Thomas Godfrey, mathematician; Samuel Rhodes, mechanician; Wm. Parsons, geographer; Thomas Hopkins, President; William Coleman, Treasurer, and Benjamin Franklin, Secretary.

In this bevy of worthies Thomas Bond was the physician, while Phineas represented general natural philosophy.

As the years went on this Society became merged in the American Philosophical Society (1767–68), and Thomas Bond was for years its Vice-President; as before stated, he at intervals contributed to the program of the meetings, usually in the form of letters from foreign medical men or those stationed in foreign ports.

Bond was a member of the Masonic Order; in 1749 he was appointed Deputy Grand Master by Franklin.

He was also President of a Humane Society, which had as its object the restoration of the drowned.

He was among the original Trustees of the Academy, later the College of Philadelphia, and later the University of the State of Pennsylvania, from which finally came the present University of Pennsylvania.

He was one of the original members of the Board of Managers of the Pennsylvania Hospital.

B. J. C. D.

One of the common reports frequently reproduced in regard to Thomas Bond is the statement that he was appointed Professor of Clinical Medicine in 1768. It is probable that this error arose in this way: Dr. Bond was one of the Trustees of the Academy and subsequently University of the State of Pennsylvania; it was not customary at that time for a man to act both as Trustee and as professor in one of the schools; thus some years later Dr. Caspar Wistar was a Trustee of the University and yet was lecturing for some seven years before he resigned his Trusteeship and accepted the professorship. This is probably the reason that no record of Dr. Bond's appointment in the University of Pennsylvania can be found upon its minutes. I do, however, find the following in the minutes of the Trustees of the University of Pennsylvania under the date of May 17, 1768: "Dr. Thomas Bond is requested by the Trustees and Professors to continue his Clynical Lectures at the Hospital as a Branch of Medical Education adjudged to be of great Importance and Benefit to the Students." It is probable, therefore, that any appointment which came to Bond came in later years, for in 1779 the charter of the College and Academy of Philadelphia was abrogated and the University of the State of Pennsylvania began its career on October 31, 1781. On that same day "Dr. Bond is requested to unite the Lectures of the Theory and Practice of Physic with his Course of Clynical Lectures," which he accepted.

PERSONAL APPEARANCE, PORTRAITS OR PICTURES.

It is difficult to secure much of an estimate of Dr. Bond's general appearance, physique, etc. Of this Thacher (*American Medical Biography*, p. 117) says: "By nature Dr. Bond was of delicate constitution and disposed to pulmonary consumption for wh'ch he went a voyage when a young man to the Island of Barbadoes. By unremitted care to his health, the strictest attention to diet, and to guard against change of temperature and also by frequently losing blood when he found his lungs affected, he lived to an age which the greater part of mankind never reached."

Until recently it was supposed that no picture or portrait of Bond existed; Morton, in his *History of the Pennsylvania Hospital*, states that he was unable to find a picture of him; William A. Armstrong, who aided Dr. Morton, writes me that every clue was run to the ground without success; an engraving (here reproduced) has been found, but which has been objected to on the ground of the costume being of too recent a date to have been worn by Bond; it cannot be Thomas, Jr., as he died at fifty; if it is not the medical Thomas Bond, who is it?

FIG. 2.—A miniature, the back of which bears the name "Thos. Bond," found among some papers of the late Dr. William Pepper.

Until the history of this picture can be definitely ascertained I shall assume that this is the portrait of our Bond.

The second portrait has a much more uncertain history; it is the property of Dr. William Pepper, and was found

among the effects of his father, the late Dr. William Pepper; it is a painted miniature, with heavy black oval frame, on the wooden back of which is written "Dr. Thos. Bond." Accompanying it was a medallion of Dr. John Fothergill, the well-known London physician and a friend of Dr. Bond.

Nothing whatever is known about the previous history of the picture. Dr. Pepper has kindly permitted me to have it photographed, and it is here reproduced.

The signature below the first picture bears some resemblance to those of Bond's at the Pennsylvania Hospital and in the co-partnership books; this is a more carefully written signature and with less boldness; he usually signed "Th. Bond," with rather heavy lines.

The cause of Dr. Bond's death is unknown. While he was considered rather a delicate man he, however, was able to persist in his medical work until within several weeks of his death. It seems probable, therefore, that he died of some acute disease or of one of the common terminations of the aged on Friday, March 26, 1784, at the age of seventy-two. He was buried on Sunday in the burial-ground of Christ Church, at Fifth and Arch streets.

The following is a portion of an obituary notice of Dr. Bond which appeared in the *Pennsylvania Gazette* of April 3, 1784:

"A complete medical education; a natural love of science, and activity in business; an intrepidity in the undertaking of difficult cases, accompanied with uncommon success in execution; and added to these a long and increasing experience; such as perhaps became at last too fatiguing for the repose due to the close of a life devoted to honorable industry. But considering the employment of his profession as the calls of duty, he resolutely sustained the hardships of it until a few weeks of his decease, to which period, notwithstanding a constitution naturally delicate, he enjoyed a degree of health, uncommon for his years, the result of his strict temperance."

His grave, which is No 37, Section O, is marked by a low, flat marble tablet. His name, age, and date of death are still easily read, but the inscription under the name has become illegible by time. I find, however, from previous records that it read as follows:

"In Memory of Thomas Bond, M.D., who practised Physic and Surgery with signal reputation and success nearly half a Century, lamented and beloved by many, respected and esteemed by all, and adorned by literary honors sustained by him with dignity. He departed this life March 26, 1784. Aged 72 years."

He died, therefore, some few years before the foundation of this College. Had he lived he unquestionably would have been one of its founders, as he was a contemporary and friend of many of the men whose names are seen upon our Founders' Tablet.

The Managers of the Pennsylvania Hospital were careful in bestowing unnecessary compliments or flattery upon those who had been their medical advisers. I do not find in their minutes any record or memorandum of the death of either Phineas or Thomas Bond. At the subsequent meetings their successors were elected and no resolutions of sympathy, etc., were passed. On January 12, 1831, the Managers of the hospital passed the following: "Resolved, that the twenty-five foot street intended to be laid out in the preceding resolution, shall be named Bond street in grateful recollection of the early, long, and faithful services of Doctors Thomas and Phineas Bond, as physicians to this institution." This street, as you all know, extends from Ninth to Eleventh streets, between Spruce and Pine, and has been for years known to us as Clinton street. I do not know why the name was changed.

In the will of Thomas Bond proven his property is bequeathed to his wife Sarah and his sons Thomas and Venables and to his two daughters, Elizabeth Martin and Rebecca Lawrence; it was witnessed by Samuel Morris, John Swift, and Benjamin Chew. After making the ordinary bequests to his family he gave several of his negro servants their freedom. It is probable that Bond's widow, Sarah, died shortly after his death, for I discovered in the Record of Burials in Christ Church that Mrs. Bond, a widow, the husband's name, however, not given, died September 19, 1784.

The foregoing comprises what I have been able to ascertain from various sources about Thomas Bond. His interest in life was widespread, his daily round including the caring for wounds, injuries, broken bones, etc.; the diagnosis and nursing of dangerous and contagious diseases, such as typhus fever and smallpox; and between times he dabbled with philosophy and philosophers, such as Franklin and Bartram, and dined with learned men, savants.

Toward the end of a useful life he devoted his last years to the service of his country; certainly before this time much of his life had been spent in the service of the medical profession of the city of Philadelphia. I therefore consider that I am at liberty to honor him as Thomas Bond, founder of the Pennsylvania Hospital, originator of the American clinic, an upright Philadelphian, and a true patriot.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Kuhn, Rush, and Bond, have succeeded, at various times, professors whose reputation has been national, such as Barton, Wistar, Chapman, Physick, Dewees, Horner, Hare, Gibson, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, Pepper, Francis Gurney Smith, Neill, Henry H. Smith, Leidy, D. Hayes Agnew, Goodell, the younger Pepper, Stillé, and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN

METRORRHAGIA MYOPATHICA.[1]

By Brooke M. Anspach, M.D.,
Gynecologist to the Philadelphia Hospital; Instructor in Gynecology, University of Pennsylvania; Assistant Gynecologist, University Hospital.

Metrorrhagia myopathica is a form of uterine hemorrhage which is independent of the usual causes of metrorrhagia,[2] and is produced by a pathological condition of the uterine muscle.

This symptom usually manifests itself toward the close of the childbearing period. At that time excessive menstrual flow or uterine hemorrhage between the periods, in the absence of the accepted causes of this abnormality, often remains an enigma. If, in a given case, there is no new-growth of any kind, if pregnancy can be excluded, if there is no adnexal visceral or general complication, if, in short, none of the usual causes of metrorrhagia obtain—the condition is, as a rule, regarded as obscure, and variously consigned to apoplexia uteri, endometritis senilis, or preclimacteric bleeding, etc. These terms are often loosely applied. Apoplexia uteri presupposes arteriosclerotic changes in the uterine arteries, with an actual rupture of one of these unhealthy vessels. This is a very rare occurence; one such case has been recently reported by Simpson. What role arteriosclerosis of the uterine vessels plays in uterine hemorrhage is yet to be decided. Reinecke says that it alone cannot account for persistent metrorrhagia, and notes cases in which there was no metrorrhagia and yet the vessels showed arteriosclerotic changes. As will be observed from my own cases, arteriosclerosis in the uterus has not the significance it takes elsewhere. In the uterus arteriosclerosis is the result of the development and subsequent involution of the bloodvessels, indelibly associated with pregnancy and the puerperium. It occurs normally in every parous uterus, and may have no more pathological import than has the general arteriosclerosis of the aged. This point will be referred to again.

Endometritis senilis is another term under which these myopathic metrorrhagia cases are grouped. Dunning has recently written extensively upon this subject. In Dunning's cases there was hypertrophy of the mucosa, arteriosclerotic changes in the bloodvessels, and a disseminated myxomatous degeneration of the muscularis. None of these conditions warrants the title endometritis senilis. There is no lesion of the endometrium characteristic of age but atrophy, and this is normal. There is as much propriety in speaking of endometritis adolescens as of endometritis senilis, for endometritis may occur at any age, and such terms convey no suggestion of the actual morphological condition. As will be shown later, arteriosclerotic changes occur in every parous uterus. The mucoid degeneration reported by Dunning might have considerable import if it were found constantly in metrorrhagia cases of this sort. At any rate, the symptoms in Dunning's cases were due either to cystic glandular endometritis or to some disease of the muscularis; in either event endometritis senilis is an inappropriate title.

Preclimacteric bleeding is a specious term given to cases of metrorrhagia myopathica, which conveys no meaning but the period of life at which the hemorrhage occurs.

It is plain from the existence of these terms that there is a class of cases which are not very well understood and are conveniently but falsely classified. This class I have designated by their chief symptom as cases of metrorrhagia myopathica, believing that the cause lies in the uterine muscle, whether it be an actual primary disease of the part itself or a secondary lesion the result of a general condition.

What is the nature of the pathological process in the wall of the uterus? Arteriosclerosis of the uterine vessels was in the past considered to be a sufficient cause. At the present time this view is not generally accepted. Theilhaber and Meir believe that a fibrosis of the uterine musculature leads to metrorrhagia; in other words, from a disproportion between its muscular and its connective-tissue constituents the uterus loses its contractile power, and this results in congestion and hemorrhage.

Several years ago Pick published a paper in which he described minutely the elastic fibres of the uterine muscle and of the uterine bloodvessels. He found that the elastic

[1] This article will appear also in the January number of the American Journal of Obstetrics.

[2] The usual causes of menorrhagia or metrorrhagia are given by Jakesch as follows:

Local. Endometritis chronica fungosa; polyps; fibromyomata; ovarian tumors (while small).

General. Chronic nephritis; heart disease; cirrhosis of liver; typhoid; cholera; variola; scarlatina; influenza; acute articular rheumatism; hemophilia; scurvy; syphillis; (secondary and tertiary); chlorosis.

To these may be added carcinoma, sarcoma, adenomyoma, pregnancy, cystic endometritis.

tissue varies in its amount and in its form at different periods of life and in different diseases. It occurred to me that as this tissue played such a large part in the pathology of arteriosclerosis, and of the vascular system in general, it would be worth while to investigate the elastic tissue in the uteri of women the subjects of metrorrhagia myopathica.

I have studied the elastica in eighteen uteri taken from women at different periods of life, and compared them with five clinical cases of metrorrhagia myopathica which have come under my observation.

In order to present clearly what there is to be said, it will be necessary to briefly review the anatomy and physiology of the uterus so far as it bears upon this subject.

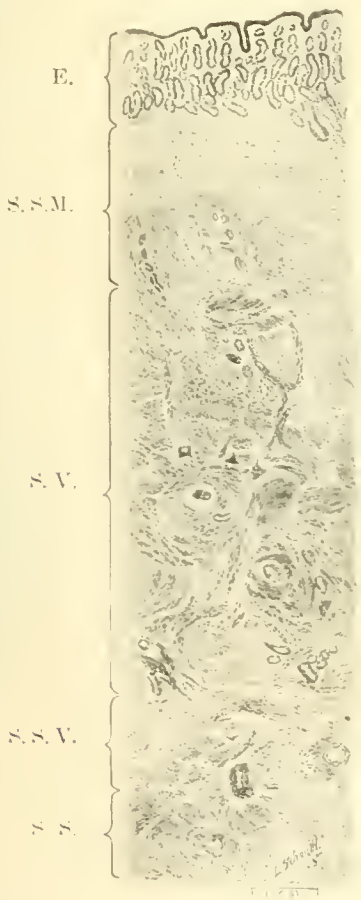

Fig. 1.—Transverse section through entire wall of nulliparous uterus at the fundus. Hæmatoxylin-eosin. Stratum subserosum (S. S.). Stratum supravasculare (S. S. V.). Stratum vasculare (S. V.). Stratum submucosum (S. S. M.). Endometrium (E.).

Anatomy. *Uterine Muscle.* The arrangement of the muscle bundles of the uterine wall has been the object of many painstaking investigations. It is exceedingly difficult to detect any very well marked division into layers, as most of the muscle bundles run indiscriminately here and there among themselves. At least this is true in the vascular layer of the uterine muscle, where the interlacing bundles of muscle surround the vascular branches upon whose calibre they are therefore able to exert a very powerful influence. Kreitzer described four layers of muscle in the uterine wall. Spohr speaks of three. The difference depends upon the degree of differentiation. If Kreitzer's classification is accepted, there is first the layer containing the large bloodvessels already mentioned, spoken of as the *stratum vasculare* (Fig. 1) Running between this and the mucosa is a layer whose general direction is longitudinal, spoken of as the *stratum submucosum.*

An outer layer running longitudinally, directly under the serous coat, is given the name *stratum subserosum.* The irregular fibres between the latter strata and the vascular layer are known as the *stratum supravasculare.* The greater part of the uterine wall, however, is made up of the vascular layer. The muscle of the uterus is of the non-striated type, intimately bound together by connective tissue which is directly continuous with the adventitia of the vessels.

Elastic Tissue. The elastic fibres of the uterus have a definite arrangement; according to Pick they have two main sources. They originate from the elastic tissue in the serous covering of the uterus and from the elastic tissue in the coats of the bloodvessel. They are very rich in the subserous and supravascular layer (Fig. 23), through which they run in a direction generally at right angles to the muscle bundles—*i. e.*, the outer or subserous layer being longitudinal and the supravascular layer being circular the main stems of elastic tissue run from the serous covering of the uterus in a centripetal direction toward the endometrium. In the vascular layer the elastica is mainly derived from the vessels and follows the ramification of the connective tissue in which it runs (Figs. 3 and 4). Exclusive of that immediately surrounding the vascular channels the amount of elastic tissue grows progressively less from the serous to the submucous coat, where there is practically none. Elastic tissue is recognized by staining with Weigert's resorcin-fuchsin stain; it appears in the form of wavy black fibres, which vary in thickness; they normally present an unbroken course, branching and rebranching until the finest subdivisions in the subserous layer surround the individual muscle cells and form elastic perimysia.[1]

Pick draws attention to the arrangement of elastic tissue in the uterus as being highly significant. The preponderance of the fibrils in the subserous and supravascular layers, their definite direction (centripetal) toward the endometrial cavity, their fine subdivision, so that in the outer layer they surround each individual muscle cell, all of this he believes shows they have a very well-defined purpose. They serve not only for the support of the blood and lymph capillaries and the nerves,

[1] The arrangement of the elastic fibres in the cervix has been studied by Dührssen. It is unnecessary to mention his paper with any detail, as the conclusions he draws deal largely with the part the cervix plays in labor.

but, further than this, they reinforce the muscular action of the uterus, protect it from being overstretched, and make easier its return to a passive state after either distention or contraction.

Bloodvessels of the Uterus. Werth and Grusdew have called attention to the vessels of the uterine wall, which are peculiar in several respects.

The larger venous branches in adult organs have a muscular wall, which runs longitudinally (Figs. 3, 10 and 11) and corresponds in its direction to the axis of the vessel. This muscular constituent of the vein they believe develops from the connective tissue of the vessel. The smaller venous channels have a very narrow or no particular wall, appearing simply as spaces separated from the musculature by a narrow layer of connective tissue.

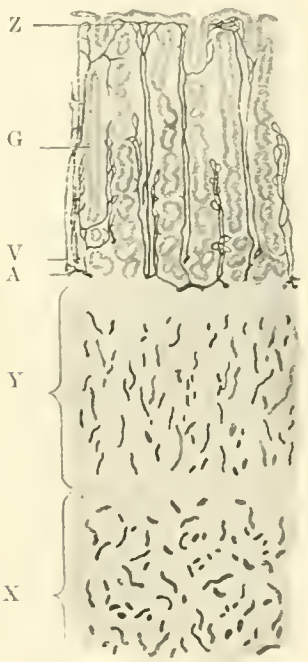

Fig. 2.—Diagrammatic scheme to illustrate vascular channels of uterine wall and endometrium. Tortuous vessels of the vascular layer (X.). Centripetal vessels of the submucosa (Y.). Subepithelial capillary plexus (Z.). Arteries (A.). Veins (V.). Glands (G.).

The arteries are distinguished by the greater breadth and consistency of their adventitia (Figs. 3 and 7). The adventitia of the larger arteries of the vascular layer contain longitudinal muscle bundles.

According to Werth and Grusdew the vascular branches of the inner part of the myometrium run directly toward the endometrium (Fig. 2). After entering the deeper portions of the mucosa the endometrial arteries give off fine, relatively large branches, which penetrate to the neighborhood of a capillary plexus (subepithelial capillary plexus) found beneath the surface epithelium. Other smaller branches pass to the glands (Fig. 2). Large venous branches lead from the subepithelial capillary plexus directly to the veins in the depths of the mucosa. There are also tributaries carrying back the blood from the capillary network directly surrounding the glands. The elastic fibres found in the vessels themselves conform to the general distribution of elastica in veins and arteries elsewhere.

Physiology. The finer physiology of the uterus embraces the changes incident to puberty, menstruation, childbirth, the puerperium, and the menopause. Physiologically the

Fig. 3. Nulliparous uterus. Area of the vascular layer, showing some of the smaller vessels. Weigert's. A., arteries. V., veins. L., lymph spaces. There is little elastica in this layer except that of the vessel walls. In the arterioles a definite internal elastic membrane can be seen; the veins show an irregular arrangement of the elastica—most of it at the periphery of the vessel. The elastica of the lymph spaces is not well formed and consists of isolated fibrils. Note the fineness of the elastic fibres and the absence of clumping. The clefts in the tissue with no elastica about them are artefacts produced by shrinkage of the tissues during the hardening.

Fig. 4.—Multiparous uterus. Area of the vascular layer, showing some of the smaller vessels. Weigert's. A., arteries. V., veins. L., lymph spaces. The increase in elastic tissue, the result of pregnancy, is at once seen when this picture is compared with Fig. 3. Observe the tendency to clumping of the fibrils.

female generative organs, especially the uterus and the ovaries, are peculiar in this, that they develop activity later than any other organ of the body, dominate in a measure all other organs for a while, and then cease their activity at a time considerably before the effects of age are noted in other

B. J. 25

parts. The changes incident to the various periods in normal uterine activity are appreciable through anatomical alterations, and these affect the several constituents of the uterine wall which have already been described.

Before the age of puberty the uterus is functionless. At puberty there begins a development of the uterine muscle. While up to that time, according to Theilhaber and Meir, but one-third of the uterine bulk is muscular tissue, the latter increases rapidly at puberty and up to the age of twenty, when the muscular elements constitute fully two-thirds of the entire bulk. There is a similar increase in elastic elements and in the vascular supply, which brings the anatomy of the uterus up to that already given of the healthy nulliparous uterus during the childbearing period.

During pregnancy all of the structures of the uterine wall undergo hypertrophy. The elastic fibres together with the other uterine tissues increase up to the fourth month.

During the latter part of pregnancy the elastic tissue diminishes, but this diminution is more apparent than real, and results from the stretching of the uterine wall.

The elastic fibres, however, increase considerably in the paracervical tissue during pregnancy, and this, it has been assumed, is a provision of nature for the dilatation of the lower uterine segment during labor. During the puerperium when all of the hypertrophied and hyperplastic elements of the uterus undergo involution, there is an actual increase in the number of elastic fibres which is sufficient to brand the parous from the nulliparous uterus (compare Fig. 3 with 4, and Fig. 23 with 24). Theilhaber and Meir assert the same of the connective tissue—viz., that while after pregnancy the entire uterus undergoes involution, this affects the muscular more than the connective-tissue elements, and results in an increase of the latter at the expense of the former. Pregnancy has an actual well-marked effect upon the vascular channels of the uterus.

Pick and Woltke have each described changes in the intima of the vessels of the vascular layer of the uterus, which occur during the puerperium.

There is a peculiar thickening of the intima, causing it to project irregularly into the lumen of the vessel (Figs. 12 and 13). This appearance they ascribe to the organization of peripheral clots. The thickened part is made up of tender elastic fibres, growing connective-tissue cells and leukocytes. A slight permanent thickening of the intima is the result. These authors have also noted a general increase of elastic tissue throughout the uterine wall, as a consequence of pregnancy and parturition. After the menopause the uterine vessels become diminished in calibre from a thickening of their walls; the vessels show more or less arteriosclerotic changes and have a tendency to approach one another to form groups. There is a great increase of elastic tissue about these groups, but the elastic fibres are mostly isolated in this position, and the islands of degenerating vessels and elastic tissue scarcely communicate with one another—so that aside from the vascular islands there is little elastic tissue in the vascular layer. In the external layers of the uterus there is also a considerable increase of the elastic tissue. This change in the proportion of elastic tissue of the uterine wall is compared by Melnikow-Raswendenkow to similar changes occurring in parenchymatous organs—*e. g.*, in the kidney, liver, heart, spleen, etc.—as the result of age. *He believes that the elastica takes the place of atrophied parenchyma, be it epithelial or muscular, and furnishes the mechanical internal equilibrium of the organ. Wherever, he says, by the atrophy of parenchymatous structures, there is a disturbance in the dynamics of secretion and excretion the vis a tergo is supplied by the new-formed elastic tissue.*

That this preservation of uterine tone is necessary during menstrual life, and that the increase of elastic tissue which accompanies the diminution of the muscle elements is a provision of nature, cannot be doubted. The contractile power of the uterus plays an important part in the phenomena of menstruation as it does in any hemorrhage from the uterus. The powerful influence which uterine contraction has upon hemorrhage from the uterine interior is seen at the close of labor. In normal menstruation the endometrium plays a passive part. There is no actual rupture of the endometrial vessels, but a diapedesis of the menstrual fluid through the thin-walled capillaries of the subepithelial capillary network. The fluid accumulates beneath the epithelium of the endometrium, and gradually finds an exit between the epithelial cells or through breaches in the epithelial layer. As this is almost entirely a passive process, it follows that the quantity of the menstrual flow is in direct relation to the blood pressure within the endometrial capillaries. The endometrial blood pressure in turn depends upon the force of the arterial supply and the calibre of the venous channels of return. As the arteries have firmer and better defined walls than the veins, they are, therefore, less compressible, and slight contractions of the uterus, which occur at the menstrual periods, would narrow the venous, but have little influence upon the arterial channels. In this way there would be a sufficient disproportion between the inward and the outward flow to produce congestion of the endometrial vessels and a resulting diapedesis. This is entirely in accord with the conclusions of Clark, who found that unless a myoma actually encroached upon and eroded the mucosa, the hemorrhage attending these tumors was due entirely to disturbances in the return circulation.

It is natural then, at the close of menstrual life, that the muscular elements having no further use should undergo atrophy, and that the intravascular area of the organ should be diminished by sclerotic changes in the bloodvessel walls, and that this should be furthered, as it is in other organs,

by an increase of elastic tissue which helps contract the vessels and takes the place of lost parenchyma. It is easy to see, therefore, that a failure in the normal increase of elastic tissue, or a failure in the normal obliterative changes of the vascular channels, or an excessive atrophy of the muscular elements, or an excessive hypertrophy of connective tissue (making firm contraction of the uterus and compression of the bloodvessels more or less faulty) might result in disturbances of the endometrial circulation and produce profuse menorrhagia or metrorrhagia.

At the University Hospital, in the gynecological service of Dr. Clark, there have been a number of cases of uncontrollable metrorrhagia. But three of these, after careful study of the cases, can be spoken of positively as metrorrhagia myopathica. In the remaining cases conditions were found after operation which might explain the trouble upon other grounds, and consequently they could not be properly regarded as myopathic. In two myopathic cases the amount of alteration in the elastica of the bloodvessels and the outer layers of the uterine wall was not in proportion to the parity of the specimen. In one case the woman had had ten children and three miscarriages; in the other two children and one miscarriage. To estimate the importance of the anatomical changes in these cases, I have studied in addition a large number of sections.

As in every investigation of this sort physiological changes are to be first recognized; eighteen uteri were selected, which had been removed at operation from patients ranging in age from seventeen to fifty-six years, and in parity from nulli to decipara. Uteri containing new-growths (carcinoma, sarcoma, or fibroid tumors) were not taken. If it had been possible autopsy specimens only would have been used. There is difficulty in securing them in sufficient number, so that I was obliged to make use of uteri removed with the adnexa in operations for pelvic inflammatory disease. The uterus in these cases is often unaffected as far as the musculature is concerned, and they were accordingly deemed suitable.

Preparation of Sections. The specimens were fixed in formalin 4 per cent., and hardened in alcohol. Either of these agents are suitable for sections to be stained by Weigert's or Van Gieson's method. After opening the uterus in each case through the anterior wall a wedge of tissue was removed below the level of the round ligament to the left of the incision. This was made to include the entire thickness of the myometrium and endometrium, and was cut at right angles to the long axis of the uterus. A second wedge was cut from the lateral wall of the cervix, just at the point of section (in supravaginal hysterectomy), or at the internal os (in panhysterectomy), including the adjacent parametrium.

This tissue was embedded in celloidin and mounted upon vulcanite blocks; sections of a uniform thickness of 30 m. were cut from each block and stored in 80 per cent. alcohol.

Thinner sections were desirable, but it was found impossible to obtain an average for the entire series less than 30 m.. Where it was expedient, serial sections of 10 m. were made. A large number of trial sections were stained by Weigert's and Van Gieson's method, in order to determine the exact technique for accomplishing the best results—that is to say, to bring out most perfectly the elastic, muscular, and fibrous tissue. It was found that the sections stained by Weigert's stain alone, without any counter-stain, exhibited best the elastic tissue, which appears intensely black in a homogeneous field. For differentiating the fibrous and muscular tissue, Van Gieson's stain, without any preparatory treatment by means of hæmatoxylin, was used. This brings out very clearly the fibrous tissue as a brilliant red and the muscle as a deep yellow.

In preparing the permanent specimens for histological examination, sections from each block were stained by Van Gieson's,[1] by Weigert's,[2] and by the ordinary hæmatoxylin-eosin methods, the technique in each case being identical.

The sections were examined with the naked eye, lying flat upon a white surface and held up to the light, and upon the stage of the microscope at a magnification of 130 and 650 diameters.

To secure accuracy in the comparison of the same slides stained by the three different methods, sketches of important fields were made by means of a camera lucida.

Observations upon the Anatomy of the Uterus. The musculature of the uterus and its bloodvessels present peculiarities found nowhere else in the body. The fibrous and muscular tissue interlace so intimately that by an ordinary hæmatoxylin-eosin stain it is difficult to differentiate between them (Fig. 1).

Vessels in Hematoxylin-eosin Preparations. The larger bloodvessels, especially the arteries, frequently run in groups (Fig. 1). The arteries are distinguishable from the veins even in hæmatoxylin-eosin preparations by a thicker wall (Fig. 5), by the circular direction of the tunica media, and by an outer fibrous coat, which sends offshoots between

[1] Van Gieson's Method. Van Gieson's stain: Saturated watery solution of picric acid, 10 parts; 1 per cent. watery solution of acid fuchsin, 1 part. This solution was freshly prepared each time; the proportions were accurately measured with a pipette. After floating the section in water it was immersed in: Van Gieson's stain, three minutes; water ten seconds; 95 per cent alcohol, one minute; absolute alcohol, two minutes; cleared in carbol-xylol and mounted in Canada balsam.

[2] Weigert's Resorcin-fuchsin Method. Weigert's resorcin-fuchsin stain: 25 c.c. of a 2 per cent. watery solution of resorcin and 25 c.c. of a 1 per cent. watery solution of fuchsin (not acid fuchsin) are placed together in a porcelain dish over a Bunsen burner. After actual boiling has started 6.25 c.c. of liq. ferri sesquichlor. (U. S. P.) are added, and the mixture is boiled for three to five minutes longer. After cooling the mixture is filtered. The filtrate is thrown away. After all the water has evaporated from the residue on the filter paper, the latter is placed in the porcelain dish first used (which has not been cleaned, and contains some of the dried precipitate of the first mixture), with 50 c.c. of 95 per cent. alcohol. This is placed over the gas flame and boiled. After the alcohol has dissolved the residue from the filter paper the latter is fished out of the solution.

The solution is allowed to cool and is then filtered. The filtrate is brought up to 50 c.c. with fresh 95 per cent. alcohol, and 1 c.c. of hydrochloric acid (C. P.) are added.

Sections were stained by placing them in Weigert's resorcin-fuchsin stain, two hours; 95 per cent. alcohol, one minute; fresh alcohol, three minutes; absolute alcohol, twelve hours; cleared in xylol and mounted in Canada balsam.

the surrounding muscle bun les. The veins in an ordinary preparation appear for the most part as clefts lined with endothelium, between diverging and converging muscular bundles. Sometimes the coat is more clearly defined and the vessel appears circular, but there is no circular direction to the tissue in its wall, and one could not say how much fibrous and how much muscular tissue its wall contained (Fig. 14).

Vessels in Van Gieson's Preparations. In sections stained by Van Gieson's method (Fig. 7) the intima and media of the arteries are yellow, while the adventitia is a brilliant red. The same color reaction distinguishes muscular from fibrous tissue throughout the specimen. The veins (Fig. 11), whether they appear as clefts between the muscle bundles or as separate structures, are seen to possess an inner coat composed mostly of fibrous tissue, in which there are muscle fibres running longitudinally in the direction of the

Fig. 5.—Nulliparous uterus. Area of the vascular layer, showing some of the smaller vessels. Hæmatoxylin-eosin. A., arteries. V., veins. L., lymph spaces. No difference can be distinguished in sections thus stained between the nulliparous and the multiparous uterus. Arteries may be distinguished from the veins by the circular arrangement of the fibres of the media. The veins show a longitudinal direction of the fibromuscular tissue forming their walls. They either have well-formed walls or appear merely as clefts between adjacent muscle bundles lined with endothelium. The smaller veins resemble the larger lymph spaces.

long axis of the vessel; and an outer coat richer in muscle and less rich in fibrous tissue, and directly continuous with or, indeed, actually a part of the surrounding musculature (Fig. 5). By Weigert's stain the elastic fibres are found throughout the muscularis. In the vascular layer they are continuations of the elastica of the adventitia of the blood-vessels. In the submucous layer they disappear outside the vessels. In the subserous and supravascular layers they pursue a centripetal direction from the serosa inward, running in fine, smooth, continuous anastomosing fibrils (Fig. 23).

The entire wall of both arteries (Fig. 6) and veins (Fig. 10) is spun through with extremely fine, anastomosing elastic fibrils; at certain parts these are thickened and form distinguishing features.

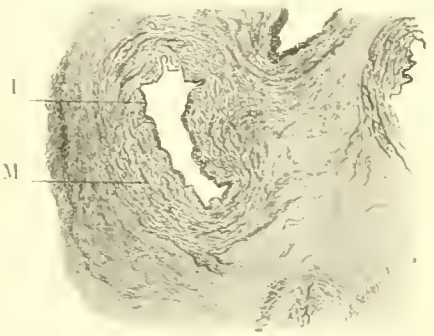

Fig. 6.—A group of arteries from the vascular layer of a nulliparous uterus. Weigert's. Note the fine, anastomosing smooth fibrils throughout the media (M.). The internal elastic membrane (I.) is well formed and regular. There is no breaking or clumping of the fibrils. Contrast this with Figs. 8, 15 and 17.

Between the intima and the media of the arteries is a wavy line of elastic tissue of especial density, which is spoken of as the internal elastic lamina. The outline of this lamina is smooth and unbroken. Between the media and the adventitia in larger vessels there is another well-formed elastic line (the external elastic lamina), but it is less marked than the internal one.

Fig. 7.—The same group of arteries as in Fig. 6. Van Gieson's. The media (M.) takes an almost uniform yellow color (muscle); A., the adventitia, a brilliant red (fibrous). Note the regular circular arrangement of the fibrous tissue lying between the circular muscle bundles of media. Contrast this with Figs. 9, 16 and 18.

The venous wall also is spun through with elastic tissue, which condenses at the border between the inner and the outer coat, although it never forms a sharp elastic lamina as is found in the arteries (Fig. 10).

The anatomical description so far applies to adult nulliparous organs. In the case of infants and children my observations agree entirely with those of Theilhaber and Meir, already given.

Features which Distinguish the Parous from the Nulliparous Uterus. There are certain departures from the nulliparous type in the arteries and in the vessels of a parous uterus which are distinctly characteristic. In every one of my cases it is easy to say, after studying a section stained by Weigert's method, whether or not the woman has had children. This is also possible, but to a decidedly less extent, in sections stained by Van Gieson's method.

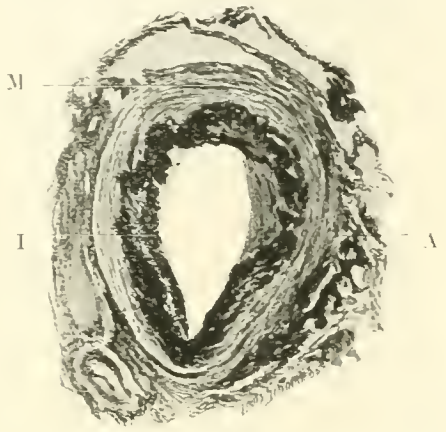

Fig. 8.—Medium-sized artery from vascular layer of multiparous uterus. Weigert's. Note the increase of elastic tissue in the media (M.) and adventitia (A.). The internal elastic lamina (I.) is greatly thickened and the fibres are broken and gathered into clumps. *Intramural arterial degeneration.* Compare with Fig. 6.

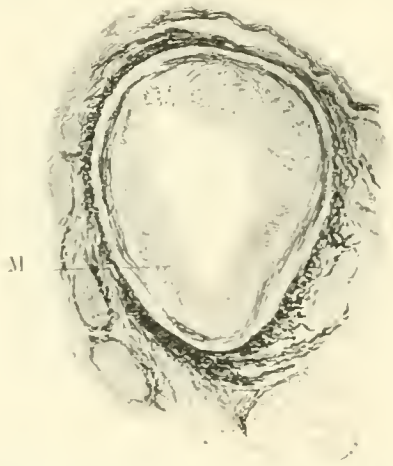

Fig. 9.—Same artery as in Fig. 6. Van Gieson's. Observe the increase of fibrous tissue (red) in the media (M.) and its irregularity. *Intramural arterial degeneration.* Compare with Fig. 7.

The changes due to pregnancy and parturition occur, as a rule, in proportion to the parity of the individual —*e. g.*, uteri repeatedly pregnant show more changes than the uteri of primipara. Similar alterations were never observed in the uteri of nullipara.

These alterations, for the sake of clearness, are taken in groups.

1. Arteries. Intramural Degeneration. *Van Gieson's Stain.* The muscle and fibrous tissue of the vessel wall no longer preserve their normal relation (Fig. 9). Deposits of fibrous tissue, red, are found within the media, and the sharp line of differentiation between the media and the adventitia is obscured. The adventitia is thickened.

Weigert's Resorcin-fuchsin Stain. The elastic tissue of the media is increased (Fig. 8), corresponding to the increase of fibrous tissue found there by Van Gieson's stain. The internal elastic lamina no longer presents its smooth, unbroken,

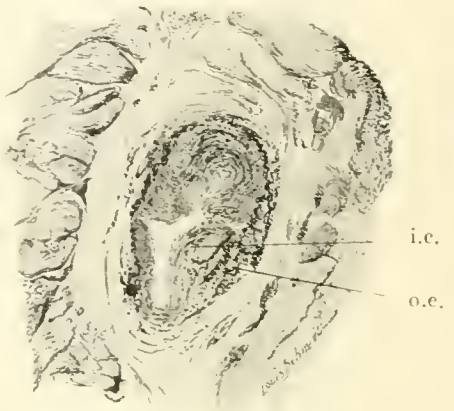

Fig. 10.—Medium-sized veins from vascular layer of nulliparous uterus. Weigert's. Observe that the inner coat (i. c.) is spun through with fine elastic fibrils; the elastic tissue is especially condensed at the border between the inner (i. c.) and the outer (o. c.) coat. It is all rather irregular, but shows no tendency to clumping. Compare this with Figs. 12 and 20.

Fig. 11.—Same vessel as in Fig. 10. Van Gieson's. The inner coat (i. c.) consists mostly of fibrous tissue (red). The outer coat (o. c.) shows muscular fibres (yellow) without any special circular arrangement; many of them are longitudinal. Compare with Figs. 13 and 21.

regularly wavy appearance. It is thickened and splits eccentrically into several layers, which are unequal in thickness and show no symmetry in form or arrangement. The elastic tissue is increased throughout the arterial wall, but

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especially in the positions already mentioned. In the larger arteries the external elastic lamina presents changes similar to those of the internal.

Hæmatoxylin-eosin Stain. The media stains like hyaline tissue and has a granular appearance, and there is a great diminution in the number of nuclei.

The changes above described are referred to in the table as *intramural arterial degeneration.*

Fig 12.—Large vein from vascular layer in multiparous uterus. Weigert's. The inner coat (i. e.) is thickened and fine elastic tissue is seen throughout; between the inner (i. e.) and the outer (o. e.) coat the elastic tissue is considerably increased and shows considerable clumping. Compare with Fig. 10.

Fig. 13.—Same vessel as in Fig. 12. Van Gieson's. The inner coat (i. e.) is irregularly thickened and the amount of fibrous tissue (red) in the vein is considerably increased. The outer coat (o. e.) shows about the proper proportion of muscle (yellow). Compare with Fig. 11.

Periarterial Degeneration. Arterial Obliteration. There is another form of change found in the arteries, especially the smaller ones of the uteri of multipara. This alteration affects principally the adventitia, but it extends finally to the entire vessel wall *and ends in complete obliteration of the vessel.*

Van Gieson's Stain. The adventitia instead of being red takes a bright-yellow stain (Fig. 16). Usually the media contains some fibrous (red) tissue. The yellow adventitia is lighter than the yellow of the muscle surrounding it, and may be thicker on one side of the vessel than on the other. It is closely connected to the surrounding tissue by a fine fibrous (red) reticulum, from which, however, it stands out prominently. Sometimes the entire vessel is represented by this bright-yellow tissue (Fig. 18), in the centre of which are a few fibrous strands (red), indicating the previous position of

Fig. 14.—Same vessel as in Figs. 12 and 13. Hæmatoxylin-eosin. The endothelial lining is very plain. No differentiation between the inner and outer coats could be made from this section. A hæmatoxylin-eosin preparation of the vein shown in Figs. 10 and 11 looked very much like this.

Fig. 15.—Group of arteries from vascular layer of multiparous uterus. Weigert's. The internal elastic lamina (i. e. l.) appears well preserved; there is no tendency to clumping of the elastic fibres in the media (M.). The adventitia (A.) presents solid clumps of elastic tissue. *Periarterial degeneration.* Compare with Figs. 6 and 8.

the lumen. Irregular patches of this bright-yellow tissue are found occasionally in the uterine wall, which represents the degenerated adventitia of a vessel cut lengthwise.

Weigert's Resorcin-fuchsin Stain. The areas described as bright yellow appear intensely black (Fig. 15). The elastic tissue occurs in irregular clumps, but these are so closely combined that the adventitia may look like a solid mass of elastic tissue.

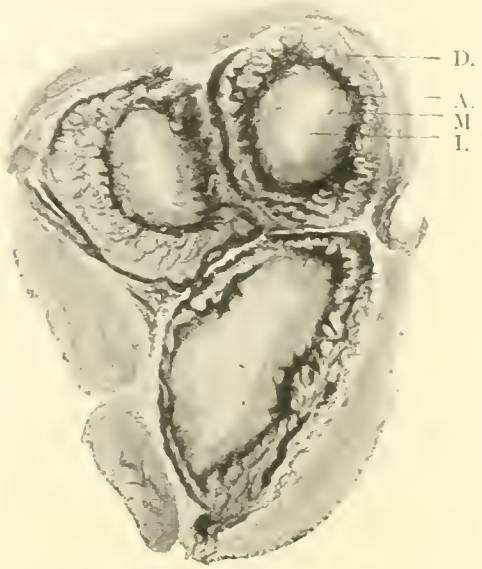

Fig. 16.—Same group of vessels as in Fig. 15. Van Gieson's. The intima (I.) and media (M.) appear practically normal; around the inner part of the adventitia (A.) is a broad ring of tissue which takes a bright yellow stain. The adventitia appears to have broadened and undergone degeneration. The degenerated (bright yellow) areas (D.) are interpenetrated by septa from the inner unehanged (red) portions of the adventitia (A.). *Periarterial degeneration.* Compare with Figs. 7 and 9.

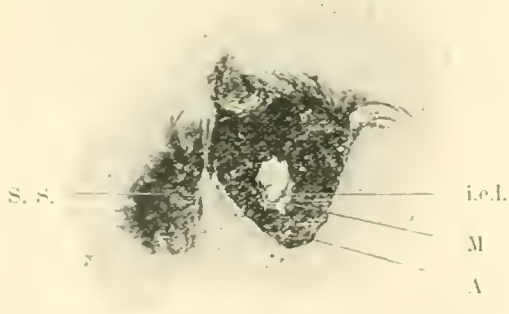

Fig. 17.—Small artery of vascular layer of multiparous uterus. Weigert's. The internal elastic lamina (i. e. l.) can still be seen in part well preserved. The adventitia (A.) and part of the media (M.) are represented by a solid mass of elastic tissue. To the left is a sagittal section through the degenerated coats of the same vessels (S. S.). *Arterial obliteration.* (Early.) Compare with Figs. 6, 8 and 15.

In the earlier cases the internal elastic lamina may be well preserved. In others it may be slightly altered. In advanced cases (Fig. 17) it is fused with the adventitial mass.

Hæmatoxylin-eosin Stain. The adventitia of the vessels has a granular hyaline appearance, in which there are few nuclei. In advanced cases (Fig. 19) the vessel is represented by a disk of this granular, hyaline-colored material, in the centre of which the lumen of the vessel can be faintly discerned lined with endothelium, or the vessel is entirely obliterated and there is no evidence of a lumen.

The advanced cases illustrate the physiological diminution of the vascular area in the uterus, which is incident to old age. Certain of the arterial branches are completely obliterated. The early changes of this sort I have designated as periarterial degeneration.

Fig. 18.—Same vessel as Fig. 17. Van Gieson's. The area represented by the elastic tissue in Fig. 16 is here of a bright-yellow color. A little fibrous tissue (red) of the adventitia (A.) and media (M.) remain. *Arterial obliteration.* (Early.) Compare with Figs. 7, 9 and 16.

Fig. 19.—Same vessel as in Figs. 17 and 18. Hæmatoxylin-eosin. The area represented by the black of Fig. 17 and by bright yellow in Fig. 18 is here pink and has a granular appearance. There are few nuclei. This is not a hyaline change as might at first appear. See Fig. 22. The adventitia of the vessels shown in Fig. 15 and 16 had this pink granular appearance in sections stained with eosin-hæmatoxylin. *Arterial obliteration.* (Early.)

2. Veins. *Van Gieson's Stain.* The internal layer (Fig. 21) becomes broader and contains more fibrous tissue; this layer takes a brilliant-red color, with occasional fine streaks of yellow. The external layer takes a light-yellow color and appears considerably broadened. There are a few fibres of fibrous tissue running through the yellow tissue, dividing it into clumps or patches. This fibrous tissue merges with the fascia of the surrounding muscle bundles. The yellow of this external layer is considerably brighter

than the yellow of the muscular tissue, and presents a striking contrast to it.

Weigert's Resorcin-fuchsin Stain. The internal layer (Fig. 20) appears spun through with delicate elastica. The external layer consists of clumps of intensely black elastic tissue, in which few individual fibres can be made out. These clumps correspond to the bright-yellow areas referred to under Van Gieson's stain.

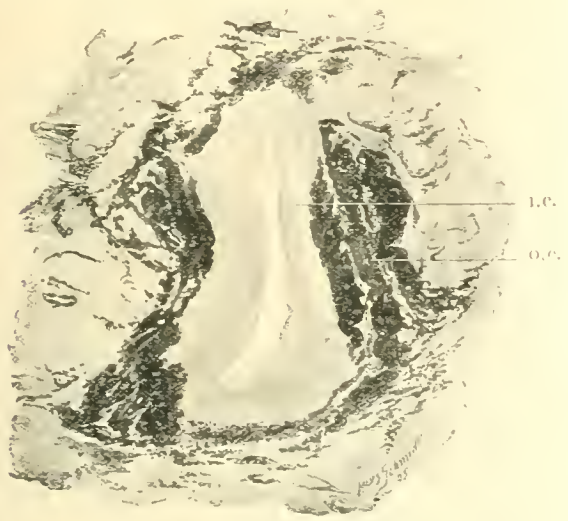

Fig. 20.—Large vein from vascular layer of multiparous uterus. Weigert's. The inner coat (i. c.) shows no change. The outer coat (o c.) is represented by large deposits of elastic tissue in clumps. *Perivenous degeneration.* Compare with Fig. 10.

Fig. 21.—Same vessel as in Fig. 20. Van Gieson's. The area of elastic tissue shown in Fig. 20 is represented here by bright yellow tissue (o. c.), which contrasts markedly with the yellow of the surrounding muscle bundles. *Perivenous degeneration.* Compare with Fig. 11.

The alteration that takes place in the veins of the parous uterus affects the smallest as well as the largest veins. The term perivenous degeneration has been applied only to the very marked cases in the large veins. The principal change is an increase of the elastica in the outer coat. This, in the larger vessels, appears light yellow by Van Gieson's stain, and has a pink, granular appearance in ordinary hæmatoxylin-eosin preparations (Fig. 22).

Hæmatoxylin-eosin Stain. The endothelial lining of the vessel (Fig. 22) can be easily distinguished by the nuclei of the cells. The tissue of the internal coat appears like ordinary fibrous tissue and has no circular arrangement. Outside of this the external coat shows a hyaline-like change, a granular red background in which there are few nuclei. This degenerated area corresponds exactly with the black of the Weigert sections and the bright yellow of the Van Gieson ones. Such changes as these are designated in the table *perivenous degeneraiton.*

Fig. 22.—Same vessel as in Figs. 20 and 21. Hæmatoxylin-eosin. The inner coat (i. c.) and the endothelial lining (e.) appear entirely normal, as in Fig. 14. The outer coat (o. c.) is represented by an area which takes the eosin (pink), has few nuclei, and is granular in appearance. See area enlarged at (X.). *Perivenous degeneration.* Compare with Fig. 14.

Relative Proportion of Fibrous and Muscular Tissue. The proportion of fibrous and muscular tissue outside the vessels as shown by Van Gieson's stain is more difficult to determine than are the changes in the elastic tissue. Van Gieson sections are judged by comparing their color under an ordinary reading glass. An estimate of the proportion of fibrous as compared to the muscular tissue is quite impracticable by any other means. Under a greater magnification one sees too little of the section at a time, and

in different fields there are different proportions, so that the only satisfactory way to get the proportion as a whole is to view the entire section and note its color. This is easily done. I took as a standard the uterus of a seventeen-year-old nulliparous girl. In this, under low magnification, about an equal mixture of yellow and red could be discerned. Cases were recorded as yellow, reddish yellow, yellowish red, and red, according to the relative proportion of fibrous and muscular tissue as shown by the color of the sections. It will be seen from the table of cases that the proportion of fibrous tissue was increased in all of the uteri where there had been multiple pregnancies, except in one case. The difference, however, is not marked, and does not seem to be as constant as the variation in elastic tissue following pregnancy. Three nulliparous uteri showed quite as much fibrous tissue as case No. 1033, where the uterus had been eight times pregnant.

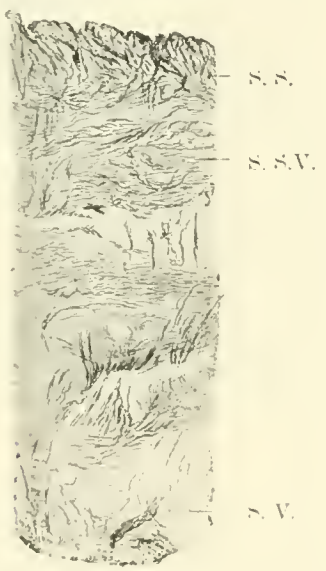

Fig. 23.—Section of wall of nulliparous uterus. Weigert's. Observe the finely branching elastica, especially marked in the stratum subserosum (S. S.). Note the general centripetal direction of the fibres. Stratum supravasculare (S. S. V.). Outer limits of stratum vasculare (S. V.).

In the cases noted clinically as metrorrhagia myopathica there was an increased amount of fibrous tissue. It is noticeable, however, that these were cases where pregnancy had occurred frequently, and that sections of uteri of equal parity contained just as much fibrous tissue, even though there had been no metrorrhagia. As said before, there is not nearly as much difference in the relative proportions of fibrous and muscular tissue between nulliparous and parous organs as was noted in respect to elastic tissue. The influence of the proportion of fibrous tissue alone, therefore, upon metrorrhagia remains doubtful. Theilhaber and Meir speak of the coexistence of an increased proportion of fibrous tissue plus an imperfect obliteration of the uterine vessels in cases of metrorrhagia myopathica at the time of the menopause. In other words, they believe an insufficient contractile power of the uterus in the presence of abnormally wide blood channels will result in hemorrhage. To actually verify an unusual width of bloodvessels is nearly physically impossible, and when the contraction that normally occurs after the action of any hardening agent is remembered any estimate is more or less unreliable. Although Theilhaber's views are logical I have not been able to verify them.

Proportion of Elastic Tissue Exclusive of that in the Vessel Walls. The amount of elastic tissue in the sections is estimated from the vascular layer and from the subserous and supravascular layers. There is no elastica outside the bloodvessels in the submucous layer. As most of the elastica of the vascular layer is derived from the outer coats of the vessels, the amount of it in each section is

Fig. 24.—Section of wall of multiparous uterus. Weigert's. Observe the clumping of the elastica; the curling and coarseness of the fibrils. Subserous layer (S. S.). Supravascular layer (S. S. V.).

indicated by the vascular changes. In the subserous and supravascular layers it can be easily estimated. The amounts and form of the elastica were judged in each case. While in the non-parous uterus the elastic fibres are smooth, more or less unbroken, and straight; in parous organs they become increased in thickness, broken, and finely curled or gathered into thick clumps. These changes are indicated for each specimen in the table. The alterations in the elastica of these outer layers are quite constant, occurring in all but two (primipara) cases of parous uteri and one multiparous organ (case of metrorrhagia myopathica).

Table of Cases of Metrorrhagia Myopathica.

Case.	Age.	M. or S.	No. of Children.	Miscarriages.	Leucorrhœa.	Menstrual flow.	Metrorrhagia.	Chief complaint.	Provisional diagnosis.	Revised diagnosis.	Thickness uterine wall.	Perivascular venous degeneration.	Intramural arterial degeneration.	Perivascular arterial degeneration.	Color by Van Gieson's stain.	Condition of elastica in subserous and supravascular layers.	State of endometrium.
1. A. L. G. No. 1528. P. No. 1070.	17	S.	0	0	Yes.	Regular, duration 7 days.	No.	Pain.	Pelvic inflammatory.	Pelvic inflammatory.	10 m.m	None.	None.	None.	Yellow and red.	Normal.	
2. C. N. G. No. 589. P. No. 428.	30	S.	0	0	No.	Regular, profuse.	No.	"	"	"	9 m.m.	"	"	"	Yellowish red.	"	
3. I. C. G. No. 822. P. No. 587.	32	M.	0	0	Yes.	Regular.	No.	"	"	"	17 m.m.	"	"	"	"	"	
4. J. McC. G. No. 613. P. No. 437.	37	M.	0	0	No.	"	No.	"	"	"	10 m.m.	"	"	"	Reddish yellow.	Clumpy.	
5. C. S. G. No. 991. P. No. 692.	37	M.	0	0	No.	Regular, profuse.	No.	Pain and menorrhagia.	"	"	19 m.m.	"	"	"	Yellowish red.	Normal.	
6. E. J. G. No. 1355. P. No. 936.	22	S.	1	0	Yes.	Regular.	No.	Pain.	"	"	19 m.m.	Slight.	Slight.	"	Reddish yellow.	Moderate increase.	
7. C. B. G. No. 1520 P. No. 1069.	23	M.	3	0	Yes.	"	No.	"	"	"	19 m.m.	Moderate.	"	Slight.	"	Slight increase, clumpy.	
8. A. P. G. No. 896. P. No. 643.	25	M.	1	0	Yes.	Regular, profuse.	No.	"	"	"	22 m.m.	Slight.	"	None.	"	Normal.	
9. A. D. G. No. 311. P. No. 254.	28	M.	1	0	Yes.	Irregular, profuse.	Occasional, slight.	"	"	"	12 m.m.	"	"	"	Yellowish red.	Slight increase.	
10. C. G. G. No. 963A. P. No. 686.	29	M.	1	0	No.	Irregular, scanty.	No.	"	"	"	16 m.m.	"	"	"	Red.	Slight increase, curly	
11. N. M. G. No. 550. P. No. 400.	31	M.	1	0	Yes.	Regular.	No.	"	"	"	12 m.m.	"	"	"	Reddish yellow.	Normal.	
12. M. H. G. No. 618. P. No. 447.	32	M.	2	0	Yes.	Regular, profuse.	No.	"	"	"	21 m.m.	"	"	"	"	Slight increase, curly.	
13. M. R. G. No. 961. P. No. 689.	35	M.	2	0	Yes.	Regular, scanty.	No.	"	"	"	14 m.m.	"	"	Moderate.	Red.	Slight increase, clumpy.	
14. E. B. G. No. 862. P. No. 618.	36	M.	8	0	Yes.	None since last labor.	No.	"	"	Puerperal metritis.	25 m.m.	Moderate.	"	Slight.	Yellow.	No increase, but curly and clumpy.	
15. S. B. G. No. 524. P. No. 382.	37	M.	4	3	Yes.	Regular.	Slight.	"	"	Pelvic inflammatory.	17 m.m.	"	Moderate.	Marked.	Yellow and red.	Slight increase, some curling.	
16. E. S. G. No. 1362. P. No. 958.	39	M.	2	8	Yes.	Irregular.	Constant.	Metrorrhagia.	Metrorrhagia myopathica.	Mitral heart disease, syphilis, cystic glandular endometritis	20 m.m.	"	"	"	Yellowish red.	Moderate increase, clumpy.	Cystic glandular endometritis following curettage
17. M. B. G. No. 568. P. No. 415.	41	M.	6	2	No.	Regular.	No.	Pain.	Pelvic inflammatory.	Pelvic inflammatory.	17 m.m.	Excessive.	Excessive.	"	Reddish yellow.	Moderate increase, curly.	
18. S. C. G. No. 762. P. No. 558.	42	M.	10	3	No.	Irregular.	Constant.	Metrorrhagia.	Metrorrhagia myopathica.	Metrorrhagia myopathica.	17 m.m.	Slight.	Slight.	None.	"	Moderate increase, very curly.	Acute septic endometritis.
19. A. C. G. No. 763. P. No. 559.	12	M.	2	1	Yes.	"	"	"	"	"	25 m.m.	"	"	"	Red.	Normal.	Normal.
20. C. H. G. No. 1152. P. No. 796.	41	M.	1	0	No.	Regular.	No.	Dysmenorrhœa	Hyperplasia uteri.	Hyperplasia uteri.	16 m.m.	"	"	"	Reddish yellow.	Slight increase, curly.	
21. W. C. G. No. 170. P. No. 93.	46	M.	8	0	Yes.	Irregular.	Constant.	Metrorrhagia.	Metrorrhagia myopathica.	Cystic degeneration of cervix, hyperplasia uteri.	25 m.m.	Excessive.	Moderate.	Excessive.	Red.	Excessive increase, clumpy.	Cystic degeneration of cervix.
22. M. B. G. No. 1176. P. No. 807.	51	M.	4	1	No.	"	"	"	"	Metrorrhagia myopathica.	21 m.m.	Moderate.	"	Moderate.	"	Moderate increase, clumpy.	Normal.
23. B. G. No. 1345. P. No. 1033.	56	M.	8	0	Yes.	Regular.	No.	Dragging pain.	Descensus uteri.	Descensus uteri.	22 m.m.	"	"	None.	Yellowish red.	Excessive increase, clumpy and curly.	

B. J. C. D.

Analysis of Cases Diagnosed Clinically as Metrorrhagia Myopathica. Before attempting to ascertain the pathology of metrorrhagia myopathica it is requisite that care be taken to exclude cases in which the origin of the hemorrhage was not strictly confined to the uterus itself. After critically examining the five clinical cases, it was found that two of them might be explained upon other grounds. A summary of the cases follows:

Gynecological No. 170; pathological No. 93. W. C., aged forty-eight years; married; eight children; no miscarriages. Always had leucorrhœa. Menstruation irregular before marriage, coming every two weeks to two months—lasting one week. Since marriage regular until eight years ago. Since then profuse menorrhagia and metrorrhagia.

Operation. Panhysterectomy. Uterus, 10 cm. long; endometrial cavity, 8 cm. long; no adhesions. Right ovary, 3 x $2\frac{1}{2}$ x 1 cm., cystic degeneration; left ovary, 2 x $1\frac{1}{2}$ x $\frac{1}{2}$ cm., atrophic. Tubes normal. Endometrium atrophic at fundus. Pronounced cystic changes in cervix and lower part of endometrium. Palpable arteriosclerosis of uterine arteries. The cystic changes in the endometrium may be responsible for the metrorrhagia in this case. I am positive that cystic endometritis may produce metrorrhagia, because I have frequently found a cystic endometritis where, from the clinical symptoms, carcinoma of the fundus was suspected and a diagnostic curettage was performed. None of these cases, so far as is known, have had a recurrence of symptoms. It is possible that the cystic changes in the endometrium are the result of some circulatory disturbance, for in one of our cases (see below) the first curettage showed the endometrium normal, while the second, several months after, found a pronounced cystic endometritis.

[I am unable to find from the history what means were employed previous to hysterectomy to control hemorrhage in this case. There is scarcely any doubt that curettage or some intrauterine treatment had been used.]

However, this first case has been classed as one of cystic degeneration of the cervix and cystic endometritis.

Gynecological No. 762; pathological No. 558. S. C., aged forty-two years; married; ten children; three miscarriages. Until three years ago menstruation regular every twenty-five days, duration seven days. No pain. For past three years, irregular every two weeks to twenty-five days. Profuse—duration seven to ten days.

Operation. Supravaginal hysterectomy. Uterus 8 cm. from point of section to fundus. Endometrial cavity 6 cm. from point of section to fundus. No adhesions. Right and left ovaries, 4 x 2 x $1\frac{1}{2}$ cm. Tubes normal. No palpable sclerosis of uterine vessels. Acute endometritis. No preliminary curettage was done in this case, and the patient died of septic peritonitis. At the time this was inexplicable. An examination of the endometrium, however, showed infiltration throughout with polymorphonuclear leukocytes. The menorrhagic symptoms cannot be explained on the grounds of an acute endometritis, for they had existed for three years, and the endometritis from the histological appearance must have been very recent. As there was no other apparent reason for the hemorrhage this case has been included under the cases of metrorrhagia myopathica.

Gynecological No. 763; pathological No. 559. A. C., aged forty-two years; married; two children; one miscarriage. Leucorrhœa at times. Metrorrhagia for two years.

Operation. Supravaginal hysterectomy. Uterus from point of amputation to fundus 10 cm. No adhesions. Endometrial cavity from point of amputation to fundus 8 cm. Right ovary, 5 x 4 x $3\frac{1}{2}$; Graafian follicle cysts. Left ovary and both tubes normal. Endometrium normal. No palpable sclerosis of uterine vessels. There is no reason to exclude this from the list of cases of metrorrhagia myopathica.

Gynecological No. 1176; pathological No. 807. M. B., aged fifty-one years; married; four children; one miscarriage. Profuse menorrhagia and metrorrhagia for past two years.

Operation. Panhysterectomy. Uterus, 8 cm. long; endometrial cavity, 6 cm. long. No adhesions. Right ovary, 3 x 2 x 1 cm., normal; left ovary, 3 x 2 x $1\frac{1}{2}$ cm., Graafian follicle cyst. Tubes normal; endometrium normal. Palpable sclerosis of uterine vessels in broad ligament. This case is included as one of metrorrhagia myopathica.

Gynecological No. 1362; pathological No. 958. E. S., aged thirty-nine years; married; two children; four miscarriages; four stillborn. Leucorrhœa constant. Menorrhagia and almost constant metrorrhagia for past year. Curettage three months before did no good. At that time examination of scrapings showed normal endometrium.

Operation. Supravaginal hysterectomy. Uterus from point of section to fundus 8 cm. Endometrial cavity from point of section to fundus 6 cm. Right ovary, 4 x 3 x 2 cm., Graafian follicle cyst; left ovary, 4 x 4 x $2\frac{1}{2}$ cm., hydrops folliculi. Tubes normal. No palpable sclerosis of uterine vessels. This case cannot be included with those of metrorrhagia myopathica because of the history of miscarriage and stillbirths, and because of mitral heart disease. The cystic degeneration of the endometrium followed the first curettage, when the endometrium appeared normal. As syphilis or heart disease might have explained this case, it has not been regarded as coming under the head of metrorrhagia myopathica.

Pathological Anatomy of Metrorrhagia Myopathica.

The results of the findings in these three cases of metrorrhagia myopathica can be seen in the table. Briefly they are as follows:

Thickness of Uterine Wall: 17, 25 and 21 mm., respectively.

Fibrous Tissue: No increase in first; marked increase in second; moderate increase in third.

Elastic Tissue: Moderate increase in first; slight in second; excessive in third.

Vascular Changes: Same degree as noted for the elastic tissue. The anatomical changes in these cases are not constant. In the first two cases the amount of elastic tissue and the vascular changes are not proportionate to the parity of the uteri. Thus in the first case the woman had had ten children and three miscarriages, and yet the changes in the elastic tissue in the vessels were not pronounced. In the second case, two children and one miscarriage, there was scarcely more alteration than is usually found in a primipara. The fibrous tissue was disproportionately increased in the second case; in the first there was not as much as would be expected from the parity of the individual. In the third case the amount corresponded to the history of the uterus.

From the first two cases it might be said that a failure of the normal increase in elastic tissue had resulted in an insufficient contractility of the uterus and a resulting congestion and hemorrhage.

Pick records a case of a woman, aged sixty-three years, who had metrorrhagia, which resisted all ordinary means of treatment. Hysterectomy (vaginal) was performed. "Outside of the somewhat arteriosclerotic vessels there was no mentionable increase of elastic tissue." From these three cases it might be inferred that a failure in the development of elastica was the essential lesion in metrorrhagia myopathica. The last case in my series, however, forbids any such conclusion at this time. To settle the question it will be necessary to study additional cases, determining first whether they actually belong under the head of metrorrhagia myopathica, excluding all other causes, general and local, before they are so classified. Although by Van Gieson's stain I have not found any fibrous-tissue changes constant, I propose to study subsequent cases after they have been prepared with Mallory's connective-tissue stain. In the present series this was impossible because the sections had not been suitably fixed.

None of the commoner forms of degeneration were present in the musculature of any of these cases; so that the myxoid degeneration found by Dunning in his series cannot be regarded as constant. Œdema was present a number of times, but as it must be regarded as the result of congestion it was not recorded. It did not occur in either of the three myopathic cases.

Conclusions. 1. Metrorrhagia myopathica stands for a *distinct class of cases*, which have heretofore been variously and incorrectly grouped under apoplexia uteri, endometritis senilis, and preclimacteric bleeding.

2. Metrorrhagia myopathica is a symptom immediately dependent upon an anatomical or a physiological lesion of the uterine muscle.

3. No anatomical lesion has as yet been demonstrated, but it will probably be found in the elastic-tissue constituents of the vessel walls and the subserous and supravascular layers.

4. The physiological lesion is most likely an insufficient contractile power of the uterus. It is possible that the condition is purely functional and that there is no anatomical change which can be recognized.

5. In cases of metrorrhagia myopathica the uterus is enlarged and softened; the os is patulous.

6. Metrorrhagia myopathica does not occur in nulliparous women, and, therefore, it must have some connection with the childbearing process.

7. The diagnosis of metrorrhagia myopathica is only justified when all other possible causes for uterine hemorrhage have been excluded. This cannot be too strongly urged, especially in reference to carcinoma.

8. The terms apoplexia uteri, senile endometritis, and preclimacteric bleeding as applied to these cases are incorrect and unscientific.

9. While curettement, atmocausis, etc., have little effect in cases of metrorrhagia myopathica, palliative measures should always be tried before adopting hysterectomy.

Obliteration of the endometrial cavity by means of destructive atmocausis is the alternative of hysterectomy in these cases. It is, however, harder to perform correctly and more dangerous than hysterectomy, which is the operation of choice.

Bibliography.

Jakesch. Ueber Menstruationsanomalien. Prag. med. Wochenschrift, Bd. xvi., Nos. 18 and 19.

Reinicke. Die Sklerose der Uterinarterien und die Klimakterischen Blutungen. Archiv f. Gynäkologie, Bd. liii.

Dunning. Senile Endometritis. Journal of the American Medical Assoeiation, vol. xliii., No. 12.

Pick. Ueber das elastische Gewebe in der normalen und pathologische veränderten Gebärmutter. Sammlung klin. Vorträge. Volkmann's, M. ccixxxiii.

Theilhaber und Meir. Die Variationen im Bau des Mesometrium und deren Einfluss auf die Entstehung von Menorrhagien und von Fluor. Archiv. f. Gynäkologie, Bd. lxvi., Heft 1.

Dührssen. Beiträge zur Anatomie, Physiologie und Pathologie der Portio Vaginalis Uteri. Archiv f. Gynäkologie, 1891, Bd. 41.

Werth and Grusdew. Untersuchungen über die Entwicklung und Morphologie der menschlichen Uterusmuskulatur. Archiv f. Gynäkologie, Bd. lv.

Kreitzer. Anatomische Untersuchungen über die Muskulatur der nicht schwangeren Gebärmutter. Landzert's Beiträge zur Anat. u. Histol., St. Petersburg, 1872.

Stöhr. Lehrbuch der Histologie und der mikrosk. Anatomie des Menschen, Jena, 1901.

Woltke. Beiträge zur Kenntnis des Elastischen Gewebes in der Gebärmutter und im Eierstock. Ziegler's Beiträge zur Pathol. Anat. u. Allgem. Pathol., 1900, Bd. xxvii. p. 575.

Melnikow-Raswendenkow. Histologische Untersuchungen über das elastische Gewebe in normalen und in pathologische veränderten Organen. Ziegler's Beiträge zur Pathol. Anat. u. Allgem. Pathol., Bd. xxvi.

Clark, John G. The Cause and Significance of Uterine Hemorrhage in Cases of Myoma Uteri. Johns Hopkins Hospital Bulletin, January, February, March, 1899. Nos. 94, 95, and 96.

Simpson, F. F. Unusual Dilatation of Cornual Blood Vessels. Rupture into Uterine Cavity; Hysterectomy; Recovery. Amer. Jour. of Obstetrics, November, 1905

FRACTURES OF THE HUMERUS BY MUSCULAR VIOLENCE.

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Fractures produced solely by muscular violence are of sufficient rarity to warrant the report of cases, especially when there is found to be no predisposing cause for their occurrence. Various diseases are known to render the individual so afflicted more liable to this accident than are the perfectly healthy. Among such affections fragilitas ossium or osteopsathyrosis is prominent. Malignant change either in the bone itself, or even in the mammary gland or the uterus, is also a not infrequent cause. Syphilis, locomotor ataxia, paresis, scurvy, and scarlet fever are among other diseases which in certain instances have been held responsible for this accident. Neither in my patient, however, not in any of those cases which are included in the tables appended to this article, were any such diseases present, all of the patients being in other respects perfectly healthy.

H. M., aged thirty-three years, came to the dispensary of the German Hospital on September 2, 1905. He stated that he had injured his arm about an hour before while playing baseball with some companions. He was throwing the ball, and as it left his hand he felt a sudden pain in the right arm, which snapped audibly and dropped helpless to his side. The ball reached its destination.

Examination of the right arm showed a fracture of the humerus just below the insertion of the deltoid muscle. The deformity was characteristic, the lower fragment being drawn up and in, while the upper was tilted outward. The patient was quite muscular, and reduction was resisted by the spasmodically contracted muscles surrounding the fracture. However, a modified Fergusson's dressing was applied, and the skiagram taken immediately thereafter by Mr. M. I. Wilbert shows that the line of fracture was nearly transverse, and that the position obtained was fairly good. The further progress of the case was uneventful, and the patient was discharged with normal functions and no palpable deformity six weeks after coming under treatment.

My purpose in recording this case, for permission to do which I am indebted to Dr. A. D. Whiting, is to call attention to the mechanism by which such fractures are produced. An examination of the recorded cases of fractures of the humerus by muscular violence shows that they are due to two main causes: first, and most commonly, to the action of throwing a ball, as in the present instance; and second, to violent twisting of the lower end of the humerus while the upper end is held rigid. This latter mode of action is seen in the contest of strength known to the French as "le tour de poignet." In this species of sport the two antagonists seat themselves at a table, on which they rest their elbows; then each endeavours by clasping the other's hand to rotate his companion's arm outward, and to bring the extensor surface of his forearm into contact with the table. To resist this outward rotation of the humerus the axillary muscles and the deltoid fix the upper extremity of the bone, and if their contraction proves stronger than the torsion elasticity of the humerus this bone will be fractured, usually a few inches above the condyles. I have collected 23 cases in which the humerus has been fractured in this manner. There are probably a few which have escaped my search, and there are certainly many which have never been reported at all.

Fracture from throwing a ball is a more common accident. I have been able to collect with little difficulty 57 cases which have been published in some detail. There are others which are merely referred to in the literature, and probably many examples of this injury have never been reported at all. Two such cases have been observed in recent years at the German Hospital in addition to that recorded in detail. In this type of fracture there are two theories of causation advocated. The original theory, said to have been proposed by Double, although his article on the subject[1] contains no clear reference to it, is that the humerus is fractured as we break a stick, by holding one end of it in our hand and whisking the other end through the air; in other words, that the projectile force given to the lower part of the arm is opposed

[1] Journ. Gén. de Méd., Chir., Pharm., etc. (Sédillot), 1805, xxiv., 376.

by the resistance of the deltoid. The other theory is that the humerus is fractured by a twist, much as in the fractures produced by the contest of strength just described. Cunningham,[1] as long ago as 1813, advocated a different theory,

H. M., Male, aged thirty-three years. Fracture of right humerus produced by throwing a base-ball. *a*, Points to fracture.

which I do not find has been accepted by any subsequent authors. He thought that in throwing a stone the dead weight of the forearm impinged on the lower end of the humerus as a blow. Apparently he means that the attachments of the biceps and the brachialis anticus act as a pivot, and that as the forearm is extended, in the act of throwing, the sigmoid cavity of the ulna strikes the trochlear surface of the humerus with considerable force, and so fractures the humerus as a fall on the hand might do. As I said, I cannot find any recent writers who agree with this explanation, even if they are aware of it; nor does it strike me as being as satisfactory as the two theories before mentioned. Indeed, as far as I can see, there is very little difference between the theory of the breaking stick and that of twisting the bone till it breaks. The only difference, I think, concerns the location of the resistive force. In the former theory the resistive force is the contraction of the muscles bringing the upper extremity of the humerus to rest, while the remainder of the limb is carried on by its acquired momentum and twists the lower part of the humerus off the upper. In the second theory the resistive force is the inertia of the whole upper extremity below the attachment of the shoulder muscles, while the fracturing force is the vigorous contraction of these muscles as they twist the upper end of the humerus off the lower.

In my own patient, and indeed in the majority of those recorded, it appears that the mechanism was of the former variety, inasmuch as the ball reached its destination. This fact shows that no fracture occurred until the hand had completed its gyrations in the air, but that the fracture occurred as the shoulder muscles attempted to bring the upper extremity to a state of rest. In a few instances, however, as in the case recorded by Lull, the ball dropped to the ground beside the player, and the arm broke just as the act of throwing was commenced. In such cases it is evident that the upper fragment is twisted off the lower, and not the lower off the upper.

In connection with these theories it is interesting to observe that the fracture is almost invariably more or less transverse, and below the insertion of the deltoid. In the case recorded by Lebeuf, however, there were two fractures in the same bone, one below the surgical neck of the right humerus, and a second fracture, oblique, at the lower third. Nelson's case was also atypical, in that the humerus was fractured very obliquely in its lower third. This patient, however, had just caught a batted ball in deep left field, and the arm broke in his attempt to return the ball to the diamond. So it is possible that the atypical injury was due to the catching of the ball, and not to the effort made to throw it.

Muscular action also at times produces fractures by tearing off a bony prominence from the humerus. Most frequently it is the internal condyle that is affected. Packard observed such a case in a woman who lifted a heavy tub. Palmer's patient tore off the greater tuberosity, and Stimson observed a similar case. Still other fractures are found

[1] N. Y. Med. Repository, 1813, n. s. i, 185.

which do not come under either of the two main headings given. Thus Cornière records the case of a young man whose humerus gave way while he was swinging from a trapeze; DeTatham notes the case of a man whose humerus was broken by pulling hard at the bridle of a runaway horse on which the patient was riding; Larrey narrates the case of a lady whose humerus gave way above the insertion of the deltoid when she grasped the handle of a carriage door; and Liston observed a fracture of the right humerus in a woman who injured herself merely by stretching out her arm to seize a child. In cases such as these special muscular forces must have been operative in every instance, and no general mode of action can be assigned.

Fractures of the Humerus by Muscular Violence.

Note.—References only to those patients who were free from constitutional and local disease are included in these tables.

I. Fractures Produced by the Act of Throwing.

1. Ashhurst, Astley: reported herewith.
2. Ashhurst, Astley: reported herewith.
3. Ashhurst, Astley: reported herewith.
4. Baffos. Arch gén. de méd., 1829, tome xxi. p. 419.
5. Bailey. Cleveland Medical Gazette, 1896-7, vol. xii. p. 33.
6. Bellamy. Lancet, 1878, vol. i. p. 699.
7. Benedikt. Wiener med. Wochenschrift, 1858, Bd. viii, S. 182.
8. Benedikt. Ibid., loc. cit.
9. Bottentuit. Journal gén. de méd., chir., pharm., etc. (Sédillot), 1805, tome xxiv. p. 375.
10. Case report in Calcutta Quarterly Journal, 1837, vol. i. p. 159, quoted in Lancet, 1837–38, vol. i. p. 566, and in Eve: "Remarkable Cases in Surgery," Philadelphia, 1857, p. 513.
11. Chaldecott. London Medical Times, 1851, n. s, vol. ii. p. 91.
12. Chamseru. Leveillé, "Nouv. Doctrine Chirurg.," Paris, 1812, T. ii. p. 166; quoted by Gurlt, "Handb. d. Knochenbrüchen," Hamm 1862, Bd. i. S. 233.
13. Chevalier. Journal de méd., chir., pharm., etc. (Boyer), 1810, T xx. p. 276.
14. Cooper, S. Dictionary of Practical Surgery, New York 1811, article: Fractures, p. 377.
15. Coots Kansas City Medical Record, 1887, vol. iv. p. 7.
16. Dumreichler. Zeitschr. d. K. K. Gesellsch. d. Aerzt zu Wien, 1858, S. 383, quoted by Gurlt, "Handb. d. Knochenbr," l. c., S. 235.
17. Dupuytren Gaz. des hôpitaux, 1833, T. vii. p. 29.
18. Ferrier. Willaume, Journ. Universel des Sc. Méd., 1818, T. xi. p. 370.
19. Frost. Lancet, 1878, vol. i. p. 737.
20. Greenwood. British Medical Journal., 1890, vol. ii. p. 1177.
21. Guthrie. American Journal of the Medical Sciences, 1835, vol. xvi. p. 524; from London Medical and Surgical Journal, May 2, 1835.
22. Haime. Jour. de la soc. méd. de Tours, 1819, 1 Trim.; also Jour. gén. de méd., 1819, T. lxviii. p. 90; quoted by Gurlt, "Handb. d. Knochenbr.," l. c., S. 233
23. Hammer. St. Louis Medical and Surgical Journal, 1853, vol. xi. p. 167.
24. Harris. Lancet, 1892, vol. ii. p. 697.
25. Hood. Australasian Medical Gazette, 1893, vol. xii. p. 361.
26. Hopkins. Philadelphia Medical Times, 1882-83, vol. xiii p. 129. Case 1.
27. Huguier. Gaz. des hôpitaux, 1854, p. 279.
28. Jacquemin. Recueil de mém. de méd., chir., et pharm. milit 1820, T. vii. p. 245.
29. Keil. Diss. Inaug., Vratislav, 1845; quoted by Gurlt, "Handb. d. Knochenbr.," l. c., S. 235.
30. Kirkbride. American Journal of the Medical Sciences, 1835, vol. xvi. p. 33.
31. Lebeuf. New Orleans Medical and Surgical Journal, 1887–88, n. s. vol. xv. p. 624.
32. Lorinser. Wien. med. Wochenschrift, 1856, Bd. vi. S. 830.
33. Lull. Southern Medicine and Surgery, Chattanooga, 1904, vol. i. p. 69.
34. Manne. Jour. gén. de méd., chir., pharm., etc. (Sédillot), 1805, T. xxiii. p. 265.
35. Melnotte. Arch. de méd. et pharm. milit., Paris, 1896, T. xxvii. p. 484.
36. Moore. Australian Medical Journal, 1895, n. s., vol. xvii. p. 495.
37. Moore. Ibid., loc. cit.
38. Nelson. Louisville Medical Monthly, 1897–98, vol. v. p. 93.
39. Nelson. Ibid., loc. cit.
40. Nelson. Ibid., loc. cit.
41. Nicolas. Union méd. de la Provence, 1866, p. 150.
42. Norris. Richmond and Louisville Medical Journal, 1872, vol. xiv. p. 498.
43. Odienne. Gaz. de Santé, I Septembre et 21 and Décembre 1817, also Hamburg. Mag. f. d. ausl. Lit. d. ges. Heilk., 1819, Bd. iii., S. 58; quoted by Gurlt, "Handb. d. Knochenbr.", loc. cit., S. 232.
44. Paine. Texas Courier Record of Medicine, Dallas, 1887–88, vol. v. p. 250.
45. Perrin. Union méd., 1857, No. 69, p. 284; also Medical Times and Gazette, 1857, vol. ii. p. 254.
46. Peyrani. Il Progresso, Giorn. Ital. d. Sc Med. e Nat., Firenze 1850, T. p. ii., 14.
47. Seaman. Vide: Cunningham, New York Medical Repository, 1813, n s vol. i. p. 183.
48. Seaton. American Journal of the Medical Sciences, 1836, vol. xvii. p. 512; from London Medical Gazette August, 1835.
49 Smith. Medical Times and Gazette, 1857, vol ii. p. 85, Case I.
50. Stephens. Transactions of the South Carolina Medical Association, 1896, p. 51.
51. Terry. British Medical Journal, 1866, vol. i. p. 518.
52. Ulrich. Gurlt, "Handb. d. Knochenbr.," Hamm 1862, Bd. i. S. 235.
53. Velpeau. Gaz. des hôpitaux, 1850, p. 76; quoted by Gurlt, "Handb d. Knochenbr.," l. e., S. 234.
54. Weist. Cincinnati Journal of Medicine, 1867, vol. ii. p. 521.
55. Wilkinson. Lancet, 1895, vol. ii. p. 733.
56. Willaume. Jour. Universel des Sc. Méd , 1818, T. xi. p. 373.
57. Withington. Boston Medical and Surgical Journal, 1897, vol. i. p. 464.

II. Fractures Produced by the Strength Test or, "Tour de Poignet."

1. Allamargot. Gaz. des hôpitaux, 1859, p. 191.
2. Brackel. Zentralblatt f. Chir., 1903, Bd. xxx. S. 512.
3. Caffort. Arch. gén. de méd., 1827, T. xv. p. 130.
4. Corbel-Lagneau. Gaz. des hôpitaux, 1846, p. 427.
5. Curtis. Boston Medical and Surgical Journal, 1878, vol. xcix. p. 479.
6. Debeaumarchef. Jour. gén. de méd., chir., pharm., etc. (Sédillot), 1805, T. xxii. p. 384.
7. Gross, S. D. System of Surgery, Philadelphia, 1872, vol. i. p. 910.
8. Gross, S. D. Ibid., loc. cit.
9. Gross, S. D. Ibid, loc. cit.
10. Hamilton. Practical Treatise on Fractures and Dislocations, Philadelphia, 1860, p. 235.
11. Laforgue. Gaz. des hôpitaux, 1851, p. 394.

12. Larrey. Annuaire méd.-chir., ou Repert. gén. de clin., Paris, 1828, S. 355; quoted by Gurlt, "Handb. d. Knochenbrüchen," Hamm 1862, Bd. i. S. 233.
13. Lasserre. Jour. Universel des Sc. Méd., 1822, T. xxviii. p. 363.
14. Lonsdale. Practical Treatise on Fractures, London, 1838, p. 165.
15. Lonsdale. Ibid., loc. cit.
16. Lucas-Championnière. Jour de méd. et de chir. prat., 1904, T. lxxv. p. 932.
17. Lucas-Championnière. Ibid., loc. cit.
18. Malgaigne. Treatise on Fractures, edited by Packard, Philadelphia, 1859, p. 429.
19. Milbradt. Berliner klin. Wochenschrift, 1902, Bd. xxxix. S. 146.
20. Monks. Boston Medical and Surgical Journal, 1895, vol. i. p. 280.
21. Monks. Ibid., 1896, vol. i. p. 41.
22 Smith Medical Times and Gazette, 1857, vol. ii. p. 85.
23. Sorensen. Hosp.-Tid., Kobenh., 1903, 4, R., xi. 915.

III. Fractures Due to Miscellaneous Causes.

1. Berncastle. Lancet, 1846, vol. i. p. 460. (Picking up a log.)
2. Cornière. Jour. de méd. et de chir. prat., 1904, T. lxxv. p. 932. (Swinging from a trapeze.)
3. De Tatham. British Medical Journal, 1890, vol. ii. p. 1126. (Pulling at bridle of horse.)
4. Giscaro. Gaz. hebdomadaire, 1856, T. iii. p. 316. (While raising body from sitting posture and leaning on arm.)
5. Hopkins. Philadelphia Medical Times, 1882–83, vol. xiii. p. 429, Case 2. (Made a miss-hit.)
6. Hopkins. Ibid., loc. cit., Case 3. (Carrying a clothes-basket.)
7. Huin. Recueil de mém. de méd., chir. et pharm. milit., 1830, T. xxix. p. 357. (Holding on hat in high wind.)
8. Larrey. Arch. gén. de méd., 1827, T. xv. p. 130. (Grasping handle of carriage door.)
9. Liston. American Journal of the Medical Sciences, 1836, vol. xviii. p. 249; Lancet, April 30, 1840. (Grabbing a child.)
10. Packard. Malgaigne's Treatise on Fractures, Philadelphia, 1859, p. 452. (Lifting heavy tub.)
11. Palmer. Journal of the Royal Army Medical Corps, London 1905, vol. iv. p. 512. (Tore off greater tuberosity of right humerus as he fell on clenched fist. Compare Stimson's case.)
12. Parker. New York Journal of Medicine, 1852, vol ii. p. 95. (A negro preacher violently gesticulating.)
13. Ravoth Gurlt, "Handb. d. Knochenbrüchen," Hamm 1862, Bd. i. S. 235. (Parrying a thrust while fencing.)
14. Smith. Medical Times and Gazette, 1857, vol. ii. p. 86. (Raising himself by arms on to wall.)
15. Stimson. Fractures and Dislocations, Philadelphia, 1899, p. 217. (Violent contraction of muscles tore off greater tuberosity. Compare Palmer's case.)
16. Velpeau. Gurlt, "Handb. d. Knochenbrüchen," Hamm 1862, Bd. i. S. 238. (Raising bucket of water from bank of stream.)

PHILIP SYNG PHYSICK: A SKETCH.[1]

By Richard H. Harte, M.D.,
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Some months ago I was asked by your President, Dr. Wharton, if I would not prepare the Annual Address in Surgery, which time-honored custom decrees shall be delivered before this body at its annual meeting. Although I naturally appreciated the compliment, I expressed to him a doubt that lay in my mind as to the value of continuing the custom, as the address robs us of much time which might be devoted to the transaction of purely scientific business, which is so important to the Academy and so valuable to the advancement of surgery in our midst. As Dr. Wharton proved obdurate, however, I undertook the task; but, as all corporate bodies are only in a measure responsible for the acts of their president, you may hold him responsible for your ennui to-night. Moreover, I am sure that the present paper will prove to you beyond cavil the the advisability of discontinuing these addresses.

In reviewing the present conditions and the history of surgery and medicine in Philadelphia, I have been led to the conclusion that we were unusually fortunate in our beginnings. The early teaching and practice of these branches here was influenced and directed by unusual men, who permanently impressed our profession for good, whose influence has descended upon us, their successors, and is still potent in the spirit that rules this Academy. Where will you find another body of men of equal size supporting themselves in the same profession, working along the same lines, in which the brotherly, manly, and disinterested spirit is more manifest than that shown in our meetings, in our discussions, and in our daily intercourse one with another? Indeed, in a long period of membership, I have never heard a single bitter or acrimonious remark during the discussions on any scientific subject in this Academy, and this spirit I largely attribute to the continuous influence of our early medical and surgical forebears in Philadelphia.

If by some Gilbertian paradox mankind in general were allowed to select their own parents, what an astonishing race of intellectual giants we should be. Genius would be the rule, rather than the exception. And yet, if we of this Academy had been allowed to choose our professional ancestors, I doubt if *we* would have been inclined to select others than those which kind circumstances accorded us. So impressed am I indeed with the far-reaching influence of those who were our pioneers and exemplars that I should like to say a word here, if you will pardon the digression,

[1] Annual Address before the Philadelphia Academy of Surgery, January 2, 1906.

about our choice of those whom we have it in our power to select as the leaders and exemplars, for those who are to follow us, and protest against the too common carelessness and indifference of governing bodies in choosing men for positions of honor or professional chairs, where, by virtue of their position and influence, they become the models and teachers of the youth of the rising generation. Too often only one qualification is demanded for such positions, that of learning or ability; whereas, in addition to these, there should equally be required those attributes of character which make the man, the teacher, and the gentleman, upon whom the searchlight of public opinion may fail to reveal any flaw in the armor of his honor. Difficult to find as such men are, they are yet the only ones fit to impress and inspire the minds of the youths who are to be the physicians and surgeons of the coming generation. The young man is most impressionable at the age when he is a student. It is then that his character is forming and takes its definite and permanent impress. It is at this period of his life that almost every youth selects for his ideal and to a certain extent patterns himself after certain types, chosen from those with whom he comes in contact. And he is particularly prone to select for imitation men recognized as leaders by the profession which he aims to follow. As the physical weakness of parents of defective vigor are reproduced in their offspring, you will find the student reproducing the moral deficiencies as well as the moral excellences of those whom you set before him as his teacher.

Now, there is abroad at the present time, seeming to imbibe and taint the very air we breathe, a widespread and apparently overwhelming desire to acquire wealth, prominence, nay, even notoriety, at any cost whatsoever. The medical and surgical professions are *not* free from this miasma, and there are those in our profession and in our city, though let me say I believe they are in the great minority, and that fortunately we do not count them as our friends, who attempt to attain those ends by methods certainly not calculated to enhance the reputation of our common profession, and none of which will be found mentioned in the code as laid down by Hippocrates.

Some of the most common of these reprehensible practices are the desire for division of consultation fees; the demand for a commission or a percentage for recommending a patient for some surgical operation; the associating with lawyers of sordid character in suits for damages against corporations, and posing as medical and surgical experts, and in this character testifying in legal cases, regardless of facts, so long as the result is favorable to their client; the clamorous announcement from the housetops, through the daily press, of some wonderful operation or invention; and last, but by no means least, the making of exorbitant charges to wealthy patients. For example, a person of reasonable means may be charged fifty dollars for some surgical procedure, and the fee may be a just and proper remuneration, but if a person of wealth consults the same practitioner for exactly the same procedure, and fails to acquaint himself in advance what the amount of indebtedness he may incur, he may learn on the receipt of his bill that he has been charged five hundred dollars, ten times the amount which was considered a full and just charge in the first instance. The bill is paid, usually without protest, but the feeling is left in the mind of the richer patient that, as a result of his known means, he has been imposed upon.

Pray, do not misunderstand me. I do not believe that we should undervalue our services. I certainly *do* believe we should be well paid for our professional skill by those who are in a position to pay us; and surely there is no class of persons in the world who give so much of their time and service gratuitously, even to those who are able to pay for it, as physicians. But, on the other hand, I must confess that I fail to see any moral difference between the man who filches a purse by force in the street and he who performs the same act of robbery under the guise of a surgical operation.

It is such practices as these—although, let me say, I believe they are comparatively few who employ them—that have brought discredit and odium on our profession and have made it a target for the butts and jibes of some of our humorous periodicals.

Now the question naturally arises, not why such things are possible, but why they are so common? Is it a native moral weakness in the offending individual? Is it the fault of defective educaton? Or is it the result of misleading example? I am inclined to regard all these as factors in the delinquencies of the few black sheep who have crept into the professional fold. If we have no control over those who bring discredit upon us through inherited or natural faults of moral nature, we certainly have the power to prevent them from transmitting these defects to the youth of our rising medical profession. I know well the feeling of every member of this Academy in regard to the practices I have just mentioned, and I know that we feel it to be our individual and collective duty to use every means to stamp out all deviations from the highest code of professional honor.

If we cannot select the natural parents of the young men who are to become our successors, we *can*, at least, select their professional parents—those who, by the prestige of high place in the profession, are to be their teachers and exemplars—by insisting that those places shall be given only to persons of unblemished character, integrity, and honor.

And this—my digression finished—brings me to that splendid band of early physicians and surgeons in Philadelphia, who have left such an indelible imprint for good

B. J. C. D.

upon our local medical character. Such names may be mentioned as Rush, Physick, Shippen, Morgan, Bond, Kuhn, Wistar, and many others. There are two contemporary names in the list which are particularly conspicuous in medical history—the names of Rush, the physician, and Physick, the surgeon.

Let me beg a share of your attention to-night for a short sketch of the latter's character;

The subject of this sketch, Dr. Philip Syng Physick, was born in the house of his father on Arch street, near Third, July 7, 1768. At that period it was considered one of the most respectable and fashionable portions of the city. His father, Edmund Physick, was an Englishman of refinement, education, and means, and during the Colonial period occupied the office known as The Keeper of the Great Seal of the Colony of Pennsylvania. After the Revolution he took charge of the estates of the Penn family, and was their confidential agent and adviser. He was a man of character and ability, and possessed some knowledge of the world. His mother was a Miss Syng, the daughter of a celebrated silversmith of this city, who was one of the early friends and companions of Franklin, and whose name appears on the Register as one of the Founders of the Philosophical Society. His grandfather was evidently largely endowed with good common sense and industry, and lived much respected by all. From him, no doubt, Physick inherited much of his manual dexterity, which stood him in good stead during many years of professional life. Dr. Physick's mother, like the mother of our beloved and esteemed late Dr. Ashhurst, was a woman of very strong religious conviction, with a firm intellect ; she evinced throughout her life great judgment and decision of character. Physick never ceased to express his filial love and reverence for his parents, attributing whatever was good and useful in his character to their example and the impressions he imbibed from them.

Little is to be learned of the boyhood of Physick. He evidently had a predilection for the mechanical arts, as we find that he made a very creditable pair of shoes, and was greatly interested in the art of the silversmith. His father, however, was determined that he should have a liberal education. He was sent at the age of eleven years to the Academy belonging to the Society of Friends in South Fourth street, under the tuition of Robert Proud. His father possessed a degree of liberality which was rather unusual at that period, always doubling the amount of the fee for his son's tuition, believing that the remuneration was not a fair equivalent for the service rendered. At this time the family resided at Lansdowne on the west side of the Schuylkill, upon an estate belonging to the Penn family. To facilitate his son's regular attendance at school his father sent him to board with the family of a Mr. John Todd. He was permitted to come home every Saturday, returning early the following Monday. Frequently he was compelled to walk to town, sometimes through most inclement weather. Notwithstanding this he always presented himself promptly at school. His punctuality was frequently commented upon by his teachers, and he was held up as an example to the other boys. Physick remained at this Academy until he entered the collegiate department of the University of Pennsylvania, where he graduated with the degree of B.A. in 1785, at the age of seventeen years.

One month after his graduation from college we find Physick entered as a student of medicine under the instruction of Adam Kuhn, a man of great learning, who had studied botany at the University of Upsal under the celebrated Lennæus. Later Kuhn also studied in London and Edinburgh, where he received the degree of M.D. After visiting France, Holland and Germany, he had returned to America and filled many positions of honor, as professor of botany in the University of Pennsylvania, and physician to the Pennsylvania Hospital. He was one of the Founders of the College of Physicians, the Philosophical Society, etc. The association of young Physick with such a master mind undoubtedly proved a great factor in the modelling of his character. Just why he decided to study medicine is not known, but I think that there is little doubt that the English method was the one adopted, *i. e.* the father selected the profession rather than the son.

Physick's first introduction to the study of anatomy was the preparation of a skeleton in the medical college. This strongly excited his aversion and created a disregard for the medical profession. On returning home he implored his father to change his mind, but all in vain. Finding his father inexorable, he entered in earnest upon the study of medicine, and shortly after this skeleton-cleaning episode it was announced that an amputation of the arm was to be performed on a certain day at the Pennsylvania Hospital, and Physick was advised by his preceptor, Dr. Kuhn, to be present. Accompanied by his father he witnessed the operation, which in those pre-anæsthetic days was something of an ordeal, and well calculated to disturb the sensibilities of a much more callous person than young Physick. They had been there but a short time when he became so ill that he had to be led from the amphitheatre.

He continued his course of study under the instruction of Dr. Kuhn and also attended lectures at the University of Pennsylvania. He did not, however, graduate from the medical department of that institution. The opportunities then offered by the schools and hospitals, at that time in their infancy, were too meagre and limited to satisfy his conscience or his ambition, and he was taken by his father to London at the age of twenty-two. Fortunately for him his father's connections in London were such that he was

able to place his son under the direct care and tuition of the great John Hunter, the foremost practical anatomist, one of the ablest physiologists, and the most accomplished surgeon of the age. After his father had placed his son under Mr. Hunter and all necessary arrangements had been completed, he said to Hunter: "I presume there are some books that my son will require. I will thank you if you will mention them, that I may procure them." "Here, sir, follow me, and I will show you the books that your son will have to study." Whereupon Mr. Hunter led the way from his study to a private dissecting room. On entering it he pointed to several bodies: "These are the books," said he, "which your son will study under my direction; the others are fit for very little."

All the sources of improvement which Physick enjoyed while in the house of Hunter have not been made known. While there Jenner was his fellow-student, and between them a rivalry arose, although they were the best of friends; this friendship lasted throughout their lives. The unusual order, perseverance and industry of Hunter was a most satisfactory example for this ambitious pupil, and in these respects he soon became the rival of his master. Uninterrupted labor and study was the order of his day. All hours of the day found Physick either in the office or ampitheatre of his instructor, executing all his directions and wishes.

This untiring devotion to practical attainment, joined to a mind peculiarly adapted to this study, made him in a short time both a favorite and confidant of his teacher. This confidence and partiality was evidenced in Hunter's successful exertions in procuring for Physick the post of house surgeon at St. George's Hospital. There were many competitors for the position, and the feeling was not overly kind toward the American. After being installed he was looked upon with jealousy and suspicion. The prejudice against anything American was still rampant in the British mind, at so short a period after the Revolutionary war. The first call for a test of Physick's skill and ability was in the reduction of a dislocated shoulder, which had just been admitted to the wards. Realizing that he would receive little assistance from his house colleagues he determined to exercise skill, rather than force, in attempting the reduction. Fortunately, the accident was a recent one; the patient was placed on a stool and told to swallow a quid of tobacco, which he held in his mouth at the time of the accident. In a few minutes he became nauseated, and his muscles relaxed, during which time Physick spent in examining very carefully the character of the injury. Then, quietly placing his left hand in the axilla, and taking hold of the elbow with his right hand, and with a little circumduction and extension, he instantly replaced the head of the humerus, much to the surprise and chagrin of the discourteous onlookers.

In 1791 he received a diploma from the Royal College of Surgeons, London, after which he spent the winter in Edinburgh and received there the degree of M.D. His thesis in Latin, entitled "De Apoplexy," was dedicated, as a mark of respect and gratitude, to John Hunter. Later, Mr. Hunter invited him to take up his residence with him and become an inmate of his family, to assist him in his professional work, and to finally establish himself in London. The tempting nature of this offer and the great advantage which he might derive from accepting it did not correspond with Physick's own designs or those of his father, since it would have necessitated exile from his native country.

Physick's devotion to his beloved preceptor was most sincere and ardent; his admiration amounted to veneration, and he never ceased to consider him the greatest man that ever adorned the medical profession.

With such an equipment we find young Dr. Physick returning to America, where his father procured an office for him in this city near Third and Arch Streets. The public was slow in recognizing what was in their midst. To use Physick's own words, he walked the streets of Philadelphia, not earning sufficient money from his profession to put soles on his shoes. Such was his discouragement and dissatisfaction, that he said: "I would have sold the fee simple of my profession for a thousand pounds; retired to the country, become a farmer, and never felt a pulse again in the capacity of a physician." He spent much time, by invitation, in a fine library belonging to a Mr. Priestman. On one occasion, he said to Mr. Priestman that he would feel much more happy if he had a certain livelihood. "If you and some other families would give me regularly twenty dollars a year to act as your physician I should be satisfied. Priestman agreed to it and, being a man of influence, interested several other families in the same direction. Shortly after this a misunderstanding arose between Drs. Rush and Wistar, in consequence of which all intercourse between them, either professionally or socially, ceased. As the result of this it became necessary for Dr. Rush to engage another surgeon to perform for him the services which had previously devolved upon Wistar. This gave Dr. Physick an immediate introduction to the public. The selection and recommendation of so high and unquestionable an authority as Rush was a sure entrée to the practice of surgery. The occurrence of yellow fever in 1793 and the terrible mortality which followed induced the Board of Health to establish a special hospital at Bush Hill for the care and attention of those who were stricken with the disease. Physick volunteered for the post of resident physician, and rendered there much valuable service. He, however, did not escape an attack of the fever, which yielded, fortunately, to treatment, but which left him with an impaired digestion for the remainder of his life. However, his services to the city in that

trying time proved to his fellow-citizens his devotion to his profession, and the utter disregard of all personal consideration which might interfere with the discharge of his duties, and the fearless manner in which he exposed himself to danger to contribute to the safety of others. It was during this time that he won the respect and esteem of Stephen Girard, who, as you possibly know, had a great prejudice against physicians, thinking that he knew as much about the treatment of diseases as those who were trained for that purpose. When, however, he did make use of the services of a physician, it was always for Dr. Physick that he sent. Girard died, however, as the victim of his prejudices, as he refused to be bled until it was too late, when he was attacked with pneumonia.

After the termination of Physick's services at the yellow fever hospital, he was presented by the management with a very valuable piece of plate, with a suitable inscription.

In 1794 Dr. Physick was elected by the Managers to the post of surgeon to the Pennsylvania Hospital. This may be said to be the dawn of his surgical fame and usefulness. This appointment had considerable influence in promoting his success and leading to an extension of his professional reputation.

In a paper written by Professor Charles D. Meigs, in 1869, speaking of some of the early members of the Pennsylvania Hospital Staff, he said, in regard to Physick: "I never knew a man who knew, so thoroughly, all that he knew; it seemed as if his science and art was so ledgered in his brain that he could turn in the instant to page and line." His service in this institution continued more than twenty-two years. His manner was in the highest degree dignified and elegant. He wore his hair in the old-fashioned clubbed and powdered style, and he bore about him a sort of a traditional look which added to the respect which everywhere, in public and private, always greeted him. When he entered the amphitheatre, no matter how tumultuous or uproarious the class, in an instant all was hushed and a sign of universal approbation greeted him, as every ear and eye attentively bent to listen to the modulated tones of his voice on the most admirable illustrations of some surgical process, which he so profusely supplied.

Dr. Physick was a very marked man in our American world of surgery, a man altogether peculiar in ability. He was one of those who stamped so indelibly into the grand old Pennsylvania Hospital the legend on its name shield, "Conservatism." Physick was preëminently the surgeon, and one of the great changes that he made in American surgery at that time was the change from operation to conservatism. No surgeon ever operated more adroitly or taught the art in its highest perfection to others more conscientiously, yet his principal aim was to prevent the necessity for operation, and in this his success was preëminent. It may not be known to some of my hearers that at the beginning of the last century anatomy and surgery were united, taught from the same chair, in the University of Pennsylvania, by a professor and an adjunct. This was complained of as an incompetent provision, for teaching. As a remedy for this evil, Physick was solicited by students and the younger members of the profession, and encouraged by Rush, to open a course of independent lectures on surgery. He complied to the request, and in the year 1801-2 began to lecture in a private capacity to a large class of students for three or four winters. His ability, popularity, and rising reputation as an instructor soon brought him prominently before the medical world. It became evident to the medical faculty that his popularity as a teacher might become a central attraction for the formation of a rival school. To anticipate this the Trustees divided the chairs of anatomy and surgery and placed them under two distinct professorships. So that, in 1805, without rival or opposition, he was induced to accept the chair of surgery. In reality the chair was created for him, and it may be well said that he honored it immeasurably more than it honored him.

The introduction of Dr. Physick to a chair in the medical faculty of the University of Pennsylvania presented him to his country in a newer and richer field of action than he had previously occupied. He brought with him all the resources and competence which the station required. The duties of the arena seemed at once as familiar to him as the hospital wards or sick room—from the first step in his academical career we find him the self-possessed, self-sustained, efficient instructor. He added greatly to the standing and reputation of the University, and the classes increased enormously. All credit, however, must not be given to Physick, for he was aided by a galaxy of talent, in the persons of Rush, Wistar, Barton, Chapman, and Dorsey.

Dr. Physick was professor of surgery in the University of Pennsylvania for thirteen years, and it was during this period that he earned his title of "Father of American Surgery." He was regarded as the mouth-piece of John Hunter in America. For in his lectures, which were carefully written and read from notes, the students heard something more than theory and a mere setting forth of operations and technique; they were taken to the roots of things and made to observe, deduce, and record. He made no attempt at any oratorical display. His style might be said to have been monotonous at times; but his observations were so concise and his conclusions so invincible that a great impression was made on his hearers, who were forced to think: and when a man has arrived at a clear conviction from inferences he is apt to think well of himself and his teachers also, so the fame of the great professor spread. These lec-

tures were Physick's most conspicuous contribution to surgery, but they, unfortunately, were lost after the telling, as they were never published.

Not only had he great ability as a didactic teacher and a brilliant operator, but he was also an able mechanic. His facility with apparatus, in the line of what is now called orthopedic surgery, was equally brilliant. He possessed a sound, practical appreciation of wound healing, and much of his teachings anticipated those of Paget and Gamgee. He was constantly interested in the treatment of fractures. We all remember his modification of Desault's splint for fracture of the thigh; his internal angular splint for fractures and injuries about the elbow joint. His appliance for correcting outward displacement in Pott's fracture was similar; he also had anticipated Dupuytren. His treatment of ununited fractures by means of a seaton added greatly to his reputation. It was lithotomy, however, which gave him his greatest fame, as he cut for stone in the bladder more often than any American surgeon of the century, possibly with the exception of Dudley: Physick invented many ingenious devices to facilitate and render safe this operation. In other branches of genito-urinary surgery he was a past-master. One of his most notable cases was his successful operation on Chief-Justice Marshall for stone in the bladder, removing over one thousand calculi.

Dr. Physick proposed and introduced the use of animal ligatures for the ligation of vessels, which after a few days would be absorbed or become decomposed by the discharge from the wound. Apparently he was the only person, for a long time, who appreciated the merits of this kind of ligature material.

In 1809 he proposed an operation for the cure of artificial anus, and successfully operated on a patient at the Pennsylvania Hospital. Some years later Dupuytren unjustly claimed the credit of the introduction of this operation. Roux, his successor in the Hotel Dieu, publicly corrected the error, giving the credit to Physick.

Physick should have remained in the chair of surgery, for which he was so fitted. It seemed as if his discretion and judgment forsook him when he allowed himself to be transferred from the chair of surgery to that of anatomy. In this step his preëminence did not accompany him. Though unequalled as a surgeon, he had more than his equals as an anatomist; in fact he had many superiors. This act was a descent from his high estate and darkened the last years of his academic career.

The lack of time, this evening, forbids my dealing longer with his professional work, which naturally interests us most. It is a great loss to the profession of his time that he did not write, as many might have benefited greatly had they had an opportunity in that way to come under the influence of his master-mind. His lack of writing is a misfortune to his memory, for justice can never be done to his labors. Though his industry and skill wrought so much for the profession of his time, it is to be regretted that this wisdom and ability gained from the immortal Hunter, this mind stored with knowledge, this clear intelligence, this remarkable skill, could not have been expressed in writing. They died with the man. It has been stated by some of his contemporaries that it was modesty and timidity to appear in print which rendered him blind to what was absolutely clear to everybody else. Personally, I am inclined to think that some of this reluctance was due to ill health, as apparently he was never thoroughly strong and robust. In early infancy he suffered from inoculation of smallpox so severely that his life was dispaired of. When in St. George's Hospital he was so ill that Hunter became greatly alarmed about him. In 1793 he contracted yellow fever, and again, in 1797, from which he nearly died. In 1814 he suffered from typhus fever, which left his health very much shattered. He always had a weak, wiry pulse, and suffered greatly from the cold. During the latter years of his life his debility was so great that it was with difficulty he could get about to attend to his duties.

In 1800, at the age of thirty-two years, he married Miss Emlen, the daughter of a gentleman of learning, distinction, and wealth. He had four children. His domestic life was all that could be desired.

His death occurred in 1837, at the age of seventy years. His character as a man was pure, steady, strong, and dignified. In the morals, courtesy, and etiquette of the profession Physick was an example for all ages. To his brother practitioners he was scrupulously just and honorable; to the younger members of the profession he was always indulgent and kind. In the latter years of his life, to those who broke through his frigid reserve, he extended the council of a patriarch and the beneficence of a father. Toward empiricks, medlars, and intriguers, however, his hostility was inexecrable. He would not countenance them in any way and always avoided them as though they were a pestilence, feeling them debasers of humanity. It may well be said that with vice, dishonor, meanness, and trickery of every description Physick was resolutely and openly at war. It was his character as a man and as a surgeon which qualifies his name to be presented to all, practitioners and teachers, as an example so instructive and commanding, so worthy of imitation—yet so difficult to imitate.

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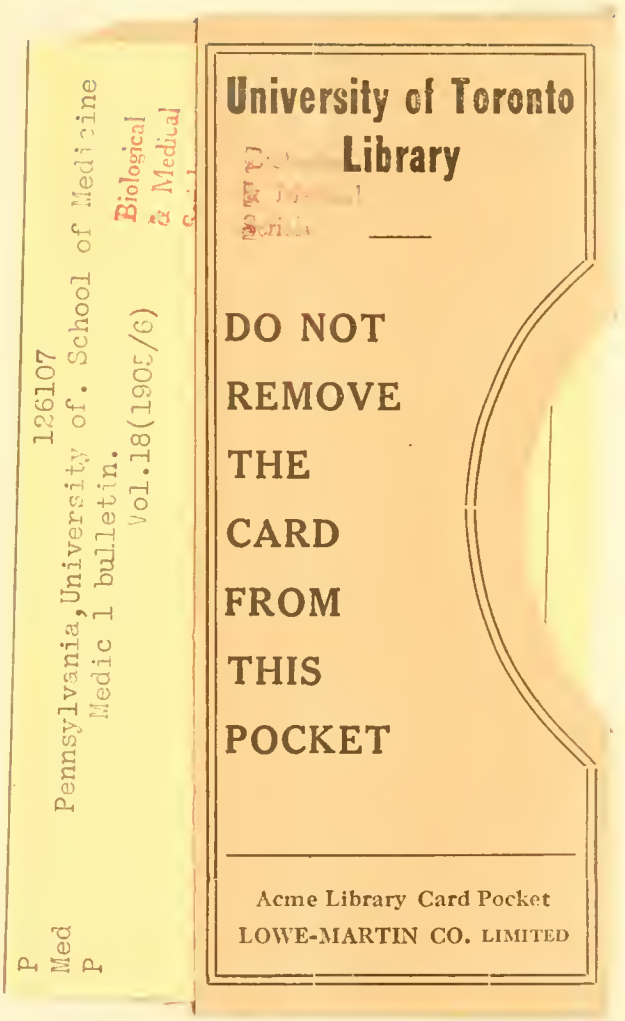
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